

Measurement of Bone Quality for CIREN and Correlation with Age and Fracture Incidence

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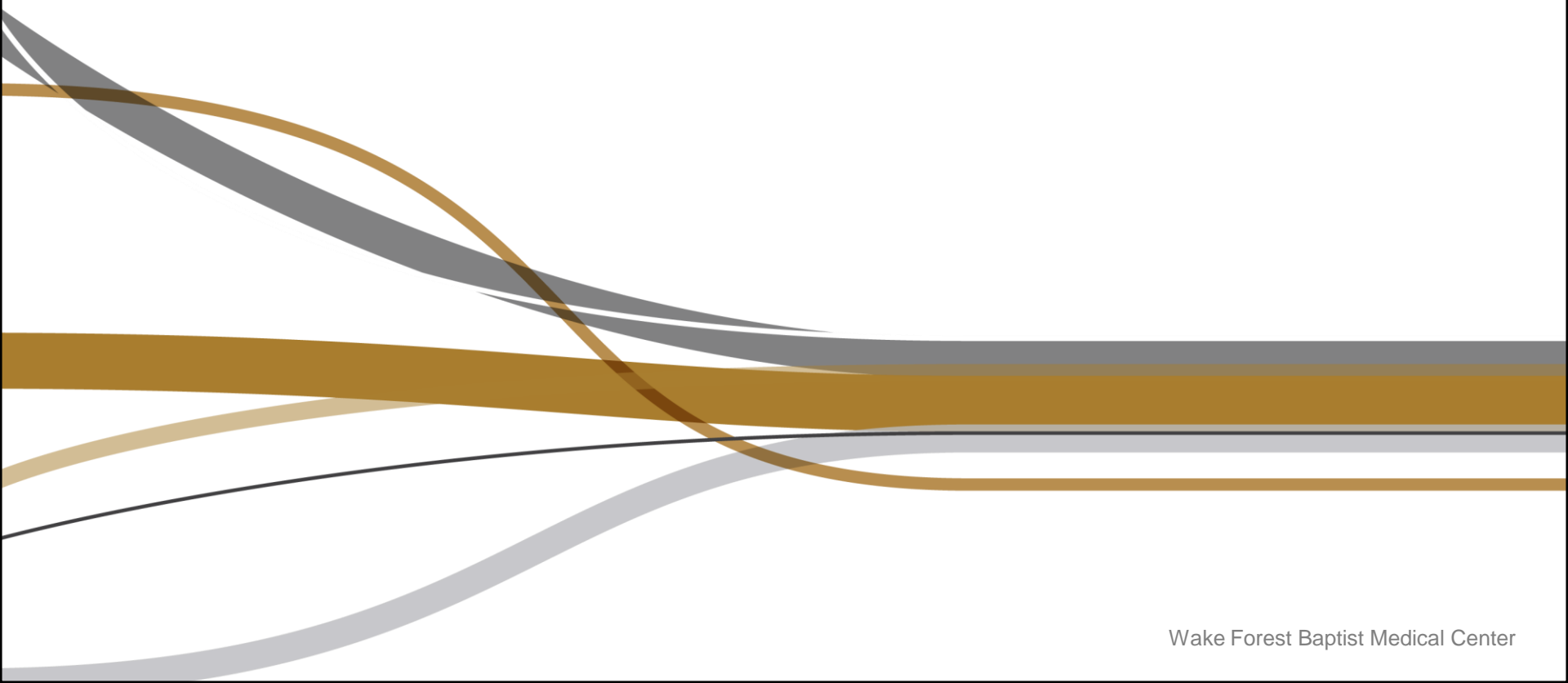
Virginia Tech – Wake Forest University Center for Injury Biomechanics, Winston-Salem, NC
Wake Forest University School of Medicine, Winston-Salem, NC

CIREN Annual Meeting
September 3rd, 2014

Center for Injury Biomechanics



Osteopenia / Osteoporosis



Public Health Concern

- 54 million Americans
- 50% of population >49 years
- 9 million fragility fractures worldwide annually
- Population continuing to age



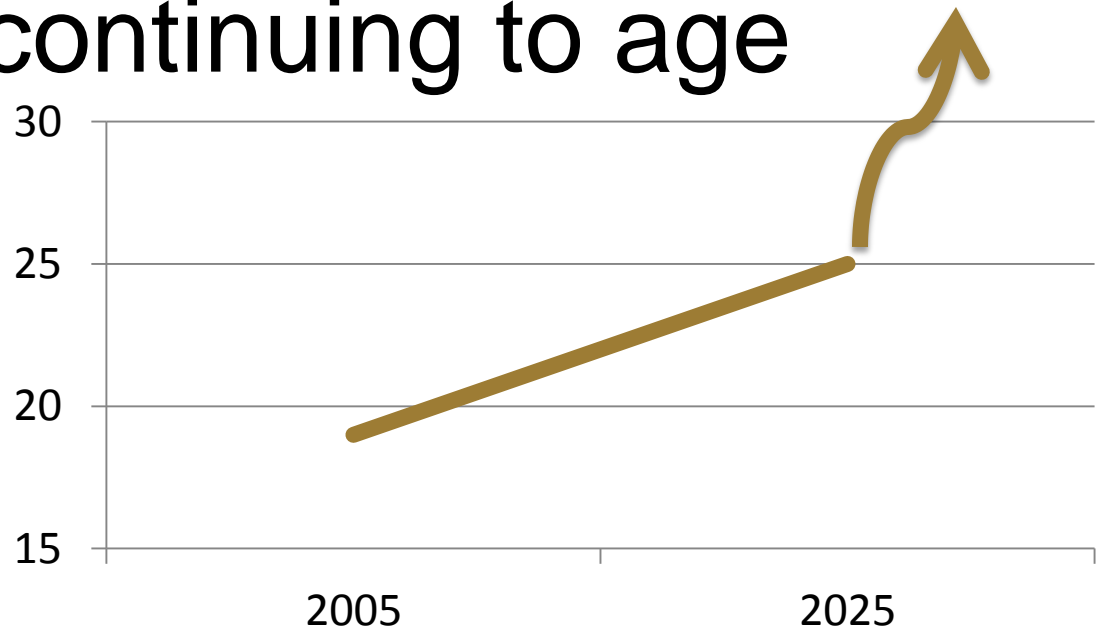
THE 12-FOOT TALL BY 12-FOOT WIDE 'CAST MOUNTAIN' PRODUCED FOR THE NBHA'S 2MILLION2MANY CAMPAIGN IS A SYMBOLIC REPRESENTATION OF THE 5500 BONE BREAKS DUE TO OSTEOPOROSIS THAT OCCUR IN THE USA EVERY DAY.

Patient Outcomes

- Decreased life expectancy
- 24% die within one year
- After one fracture, subsequent fracture risk increases 86%
- 15% readmission rate

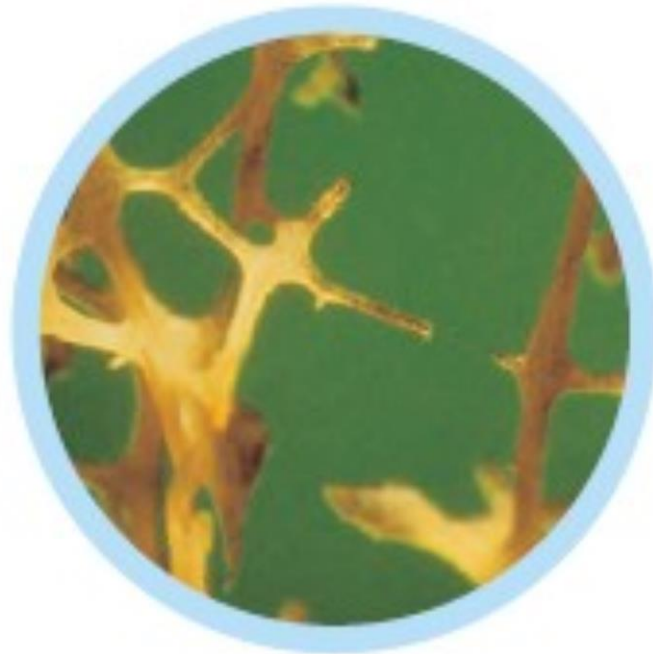
Economic Costs

- \$19 billion in 2005
- \$25.3 billion estimated by 2025
- Population continuing to age



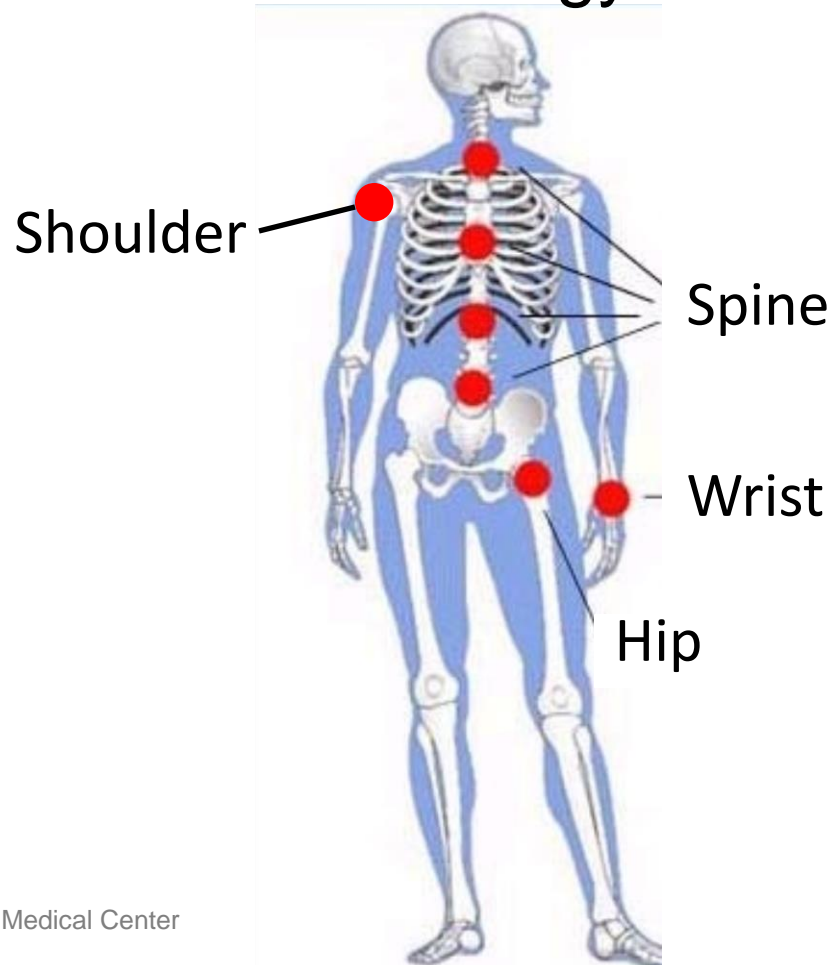
What is Osteoporosis?

- Porous bone
- Decreased density or quality



Fragility Fractures

- Fracture from low energy



Older Drivers

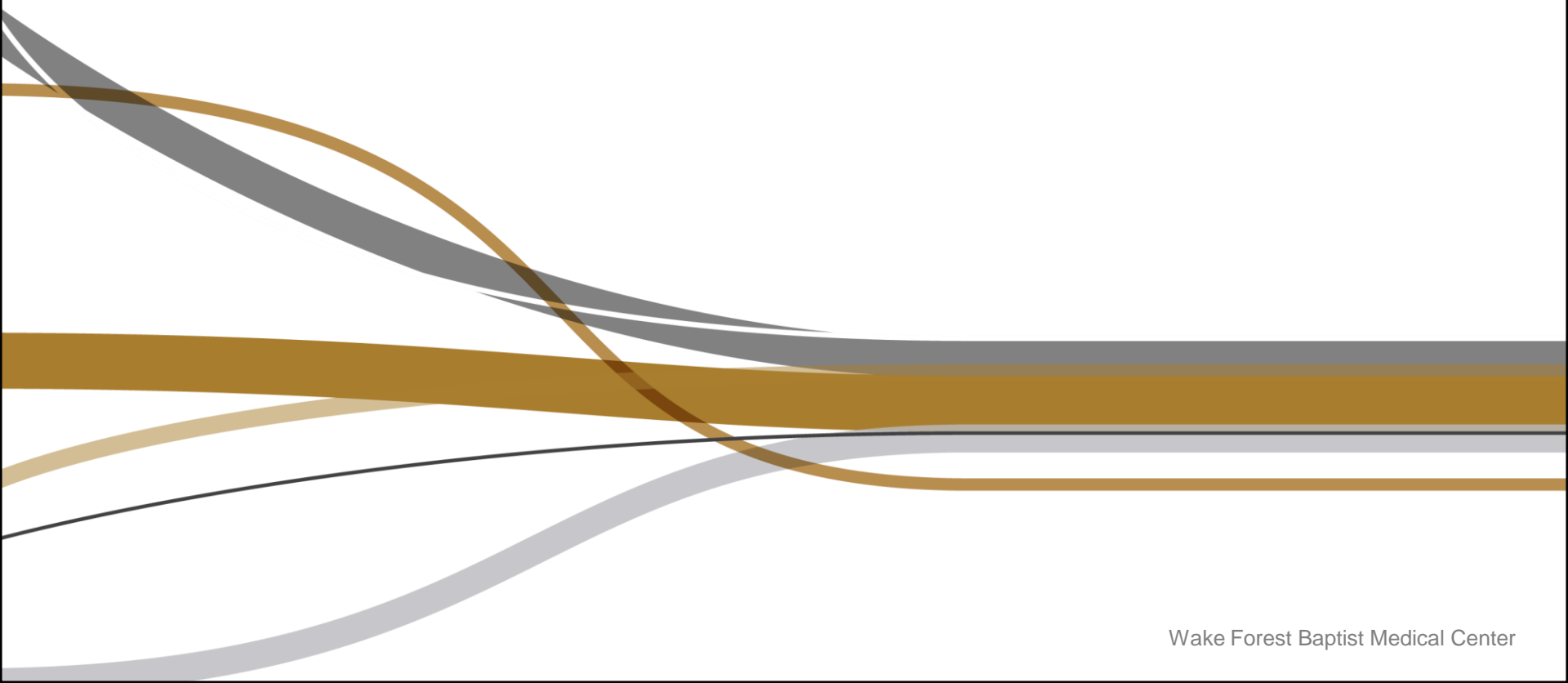
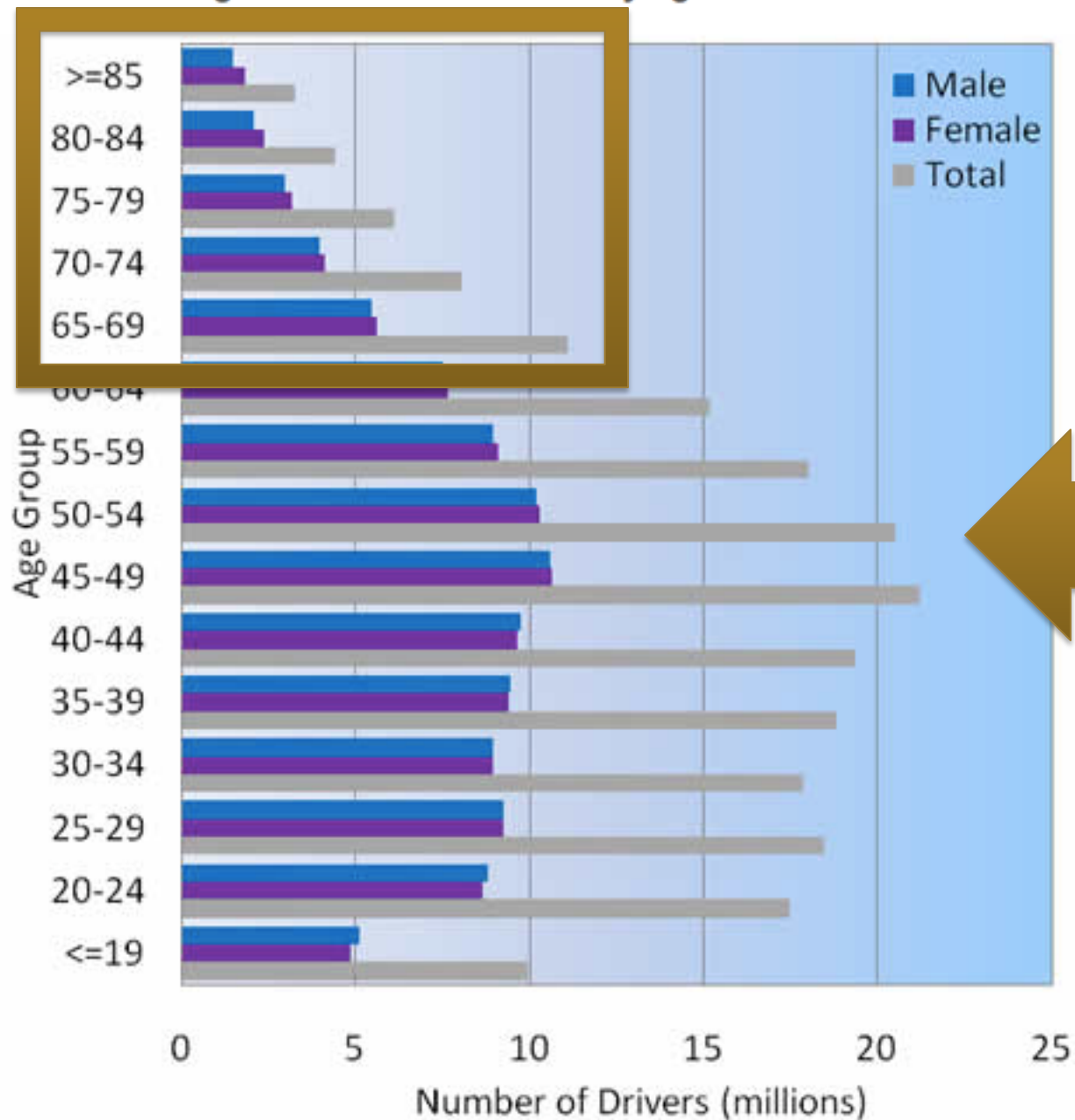
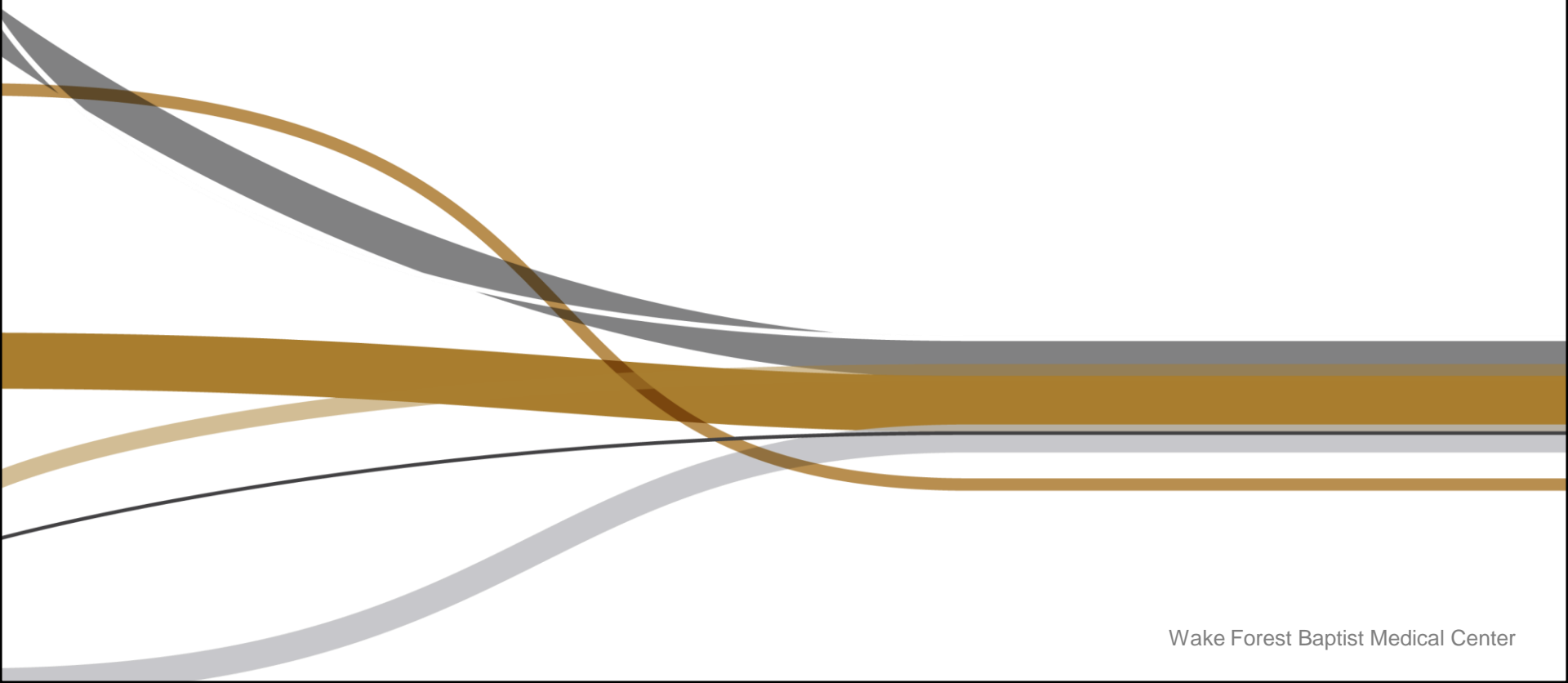


Figure 4-3: Licensed Drivers by Age and Gender: 2009

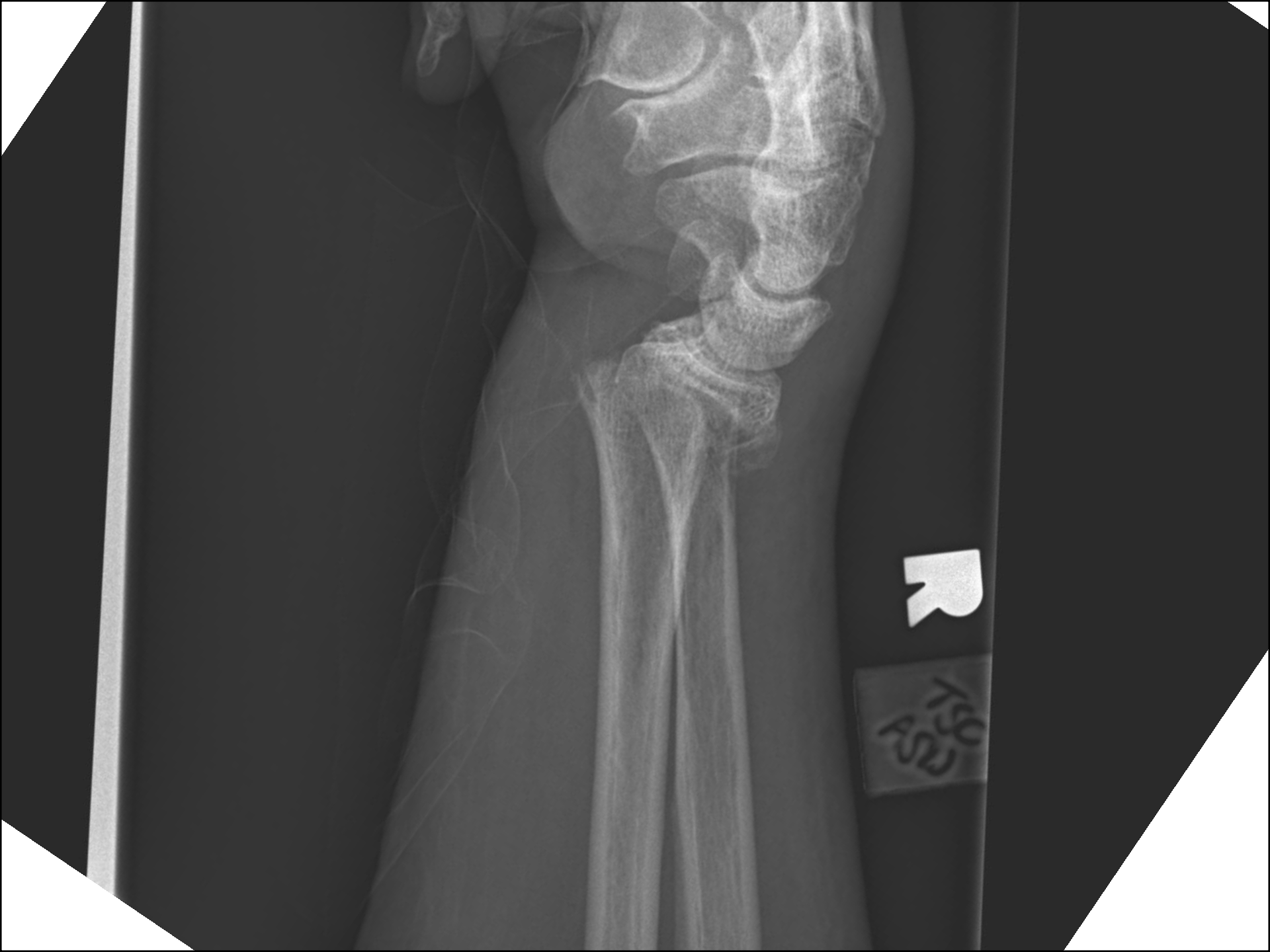


Elderly Polytrauma

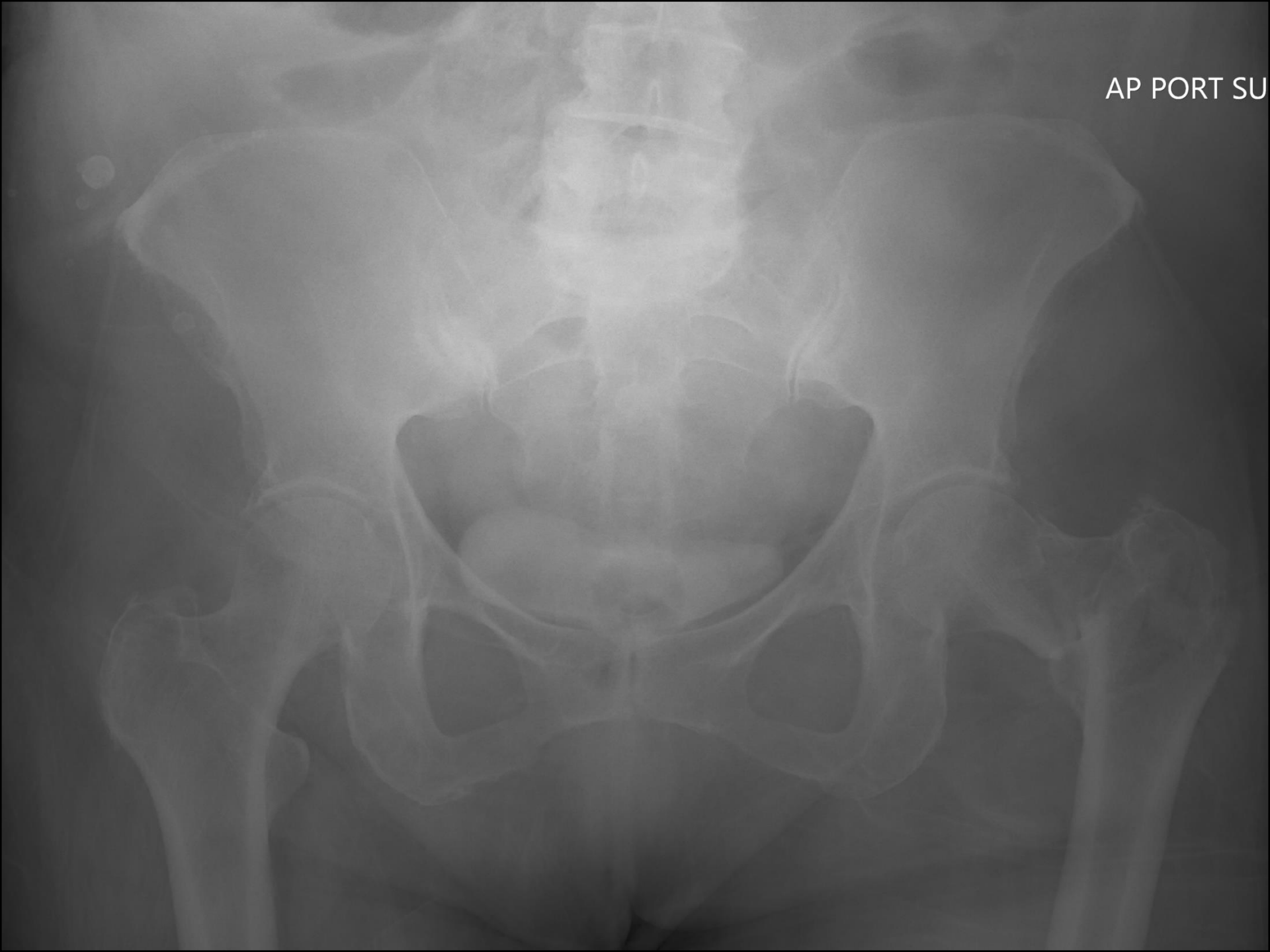


79F

- Restrained driver with grandson
- “High-speed,” head-on collision
- Hypotensive
- Pneumothorax
- Small bowel injury



AP PORT SU



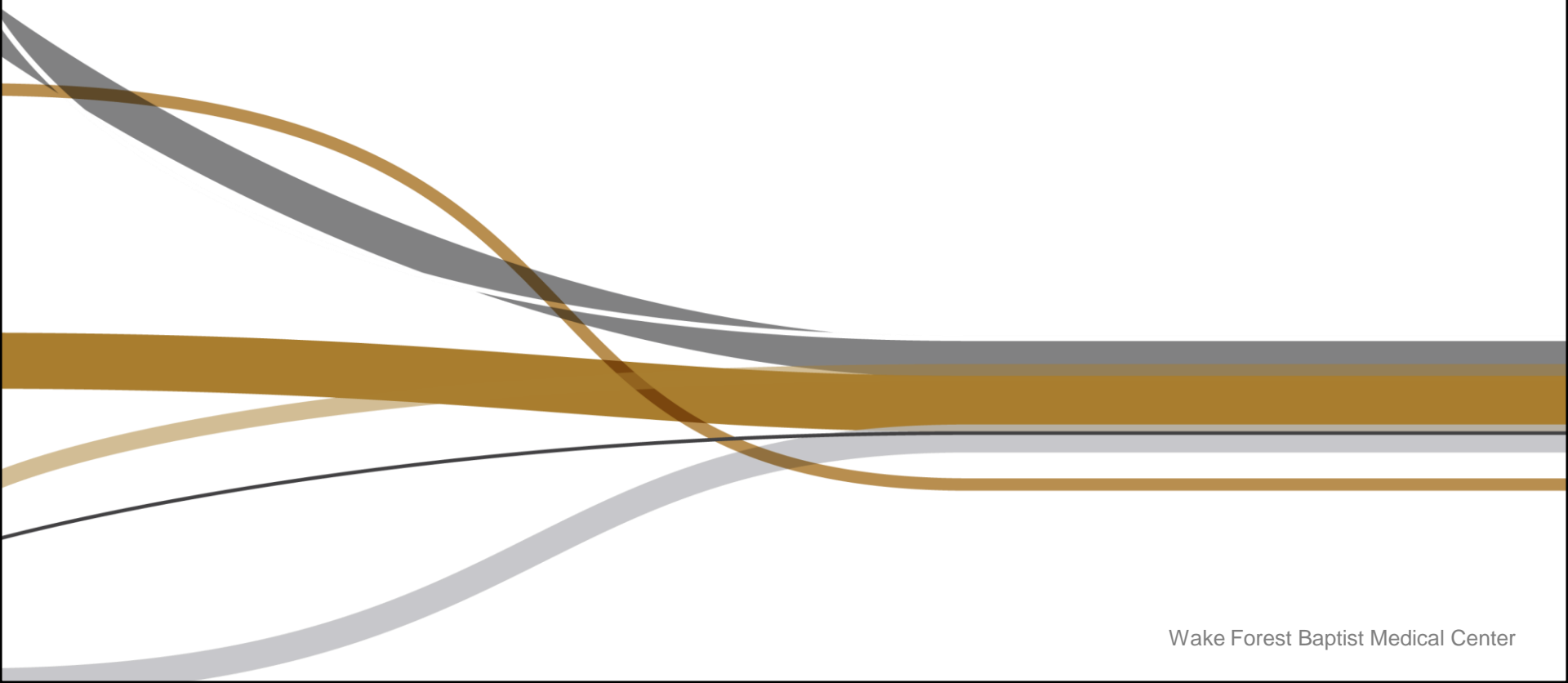
ASW

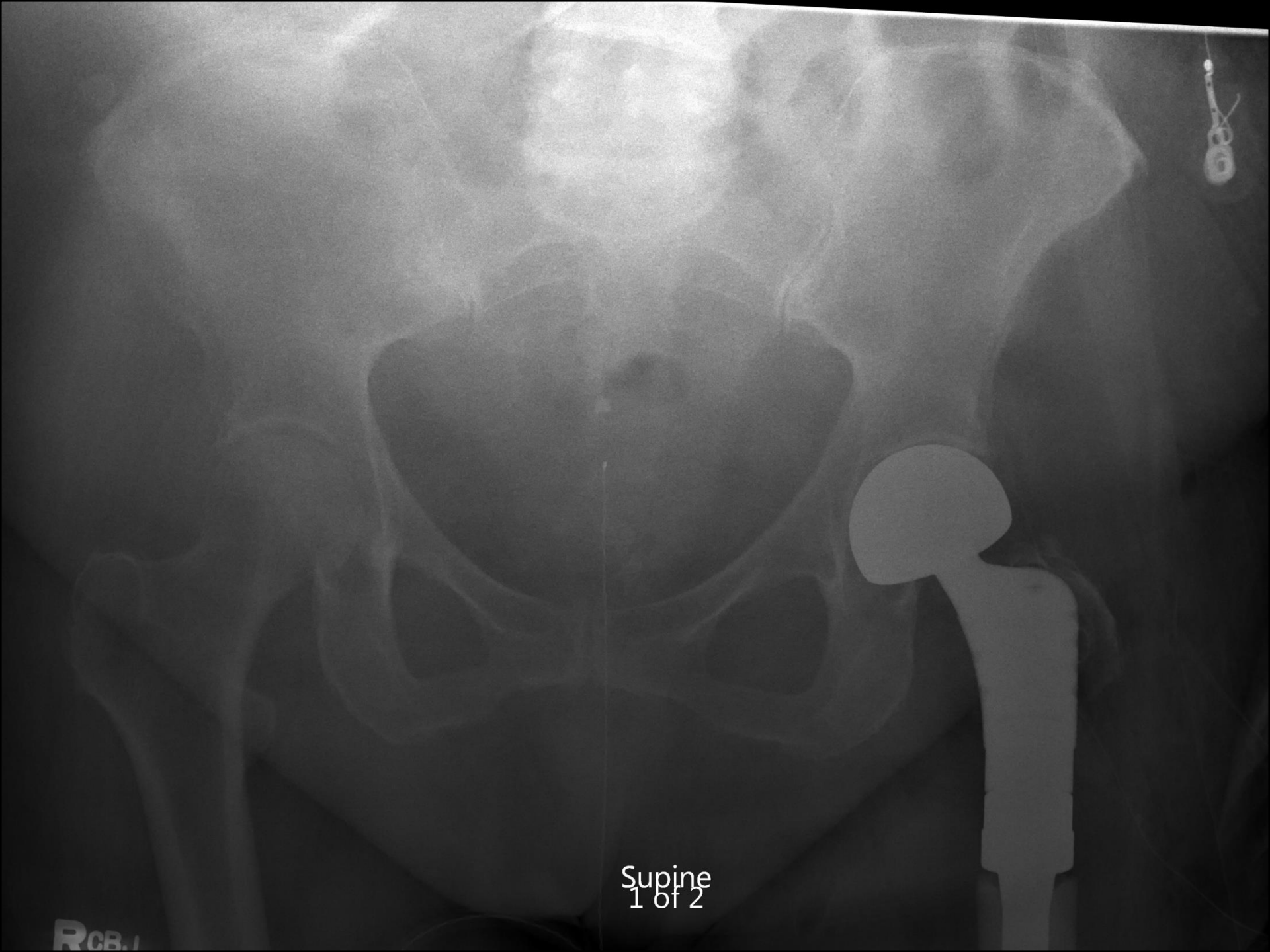


LTSC



Elderly Goals





Supine
1 of 2

RCB.1

R
KS





L
KRS

R
KS



Outcome

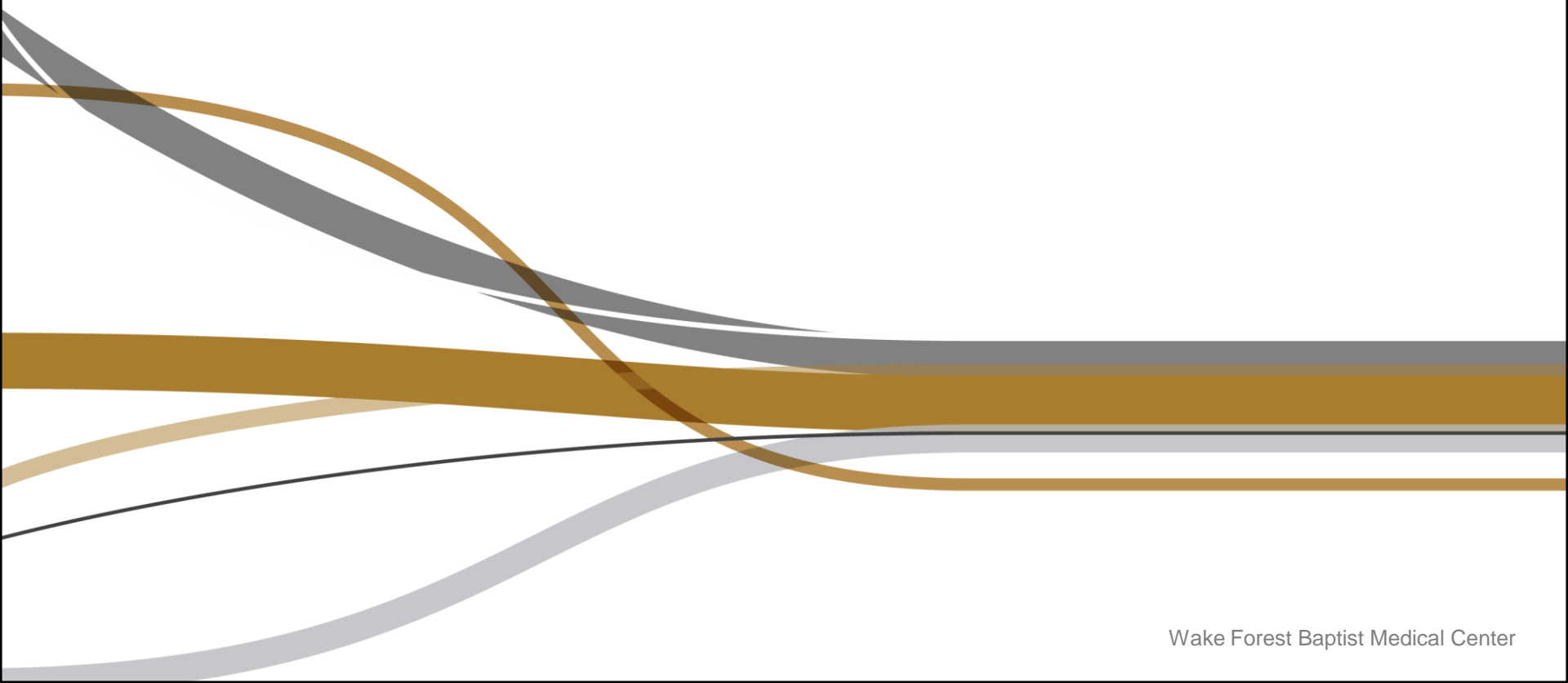
- Pneumonia
- Sepsis
- Cognitive deficit
- Hospitalized 67 days

Outcome

- By 2017 up to 11% penalty
 - Readmissions
 - Hospital-acquired conditions
- Bundled payments

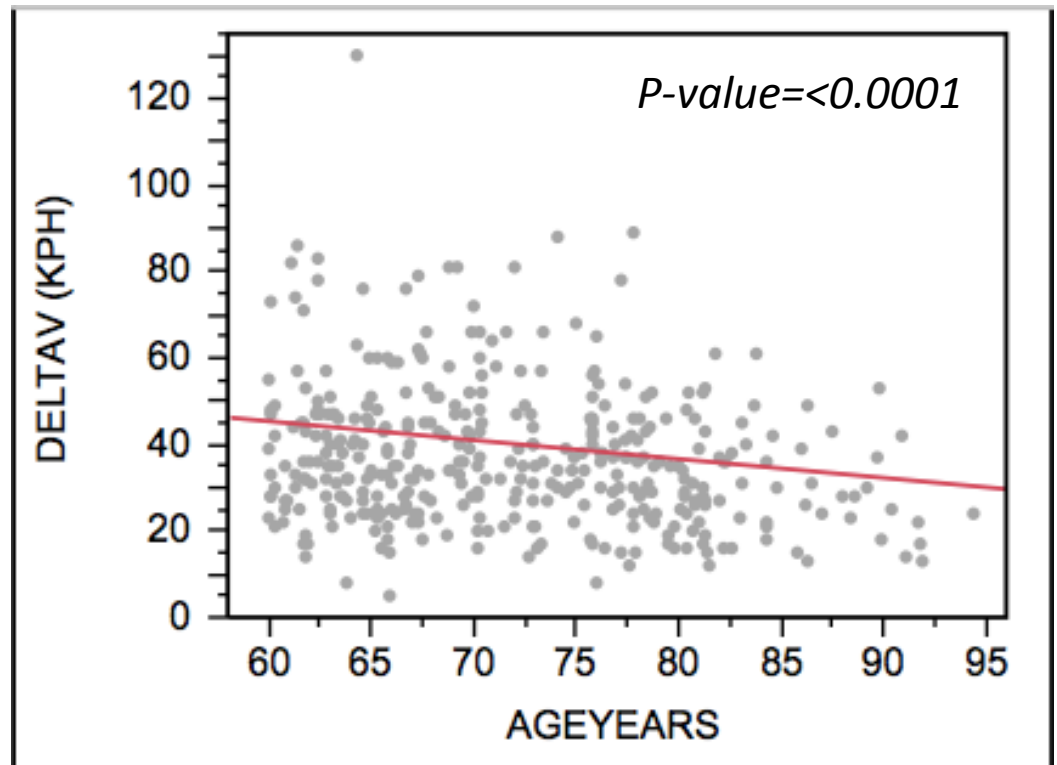


CIREN Relevance?

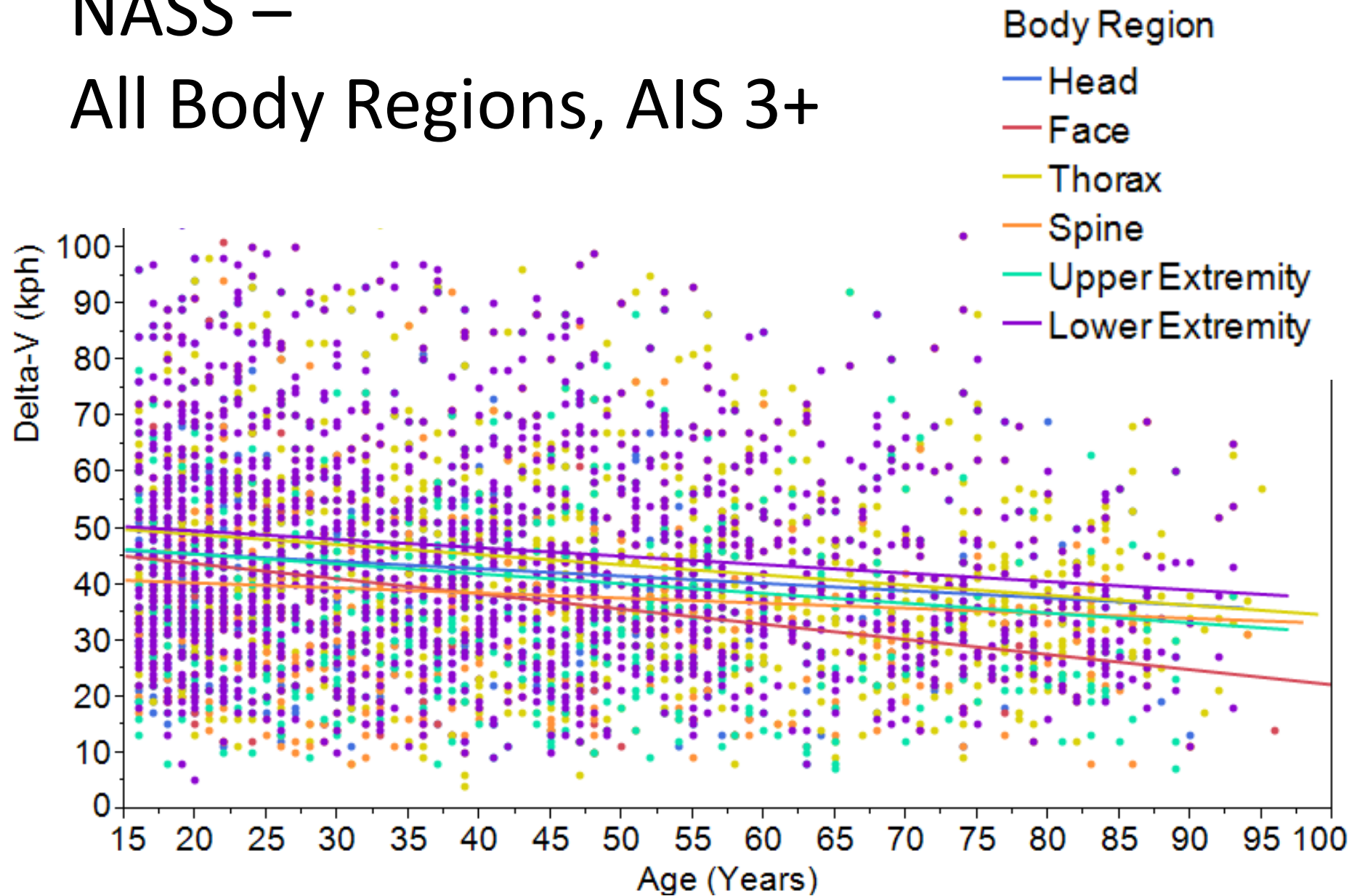


↑Fractures with ↓ ΔV

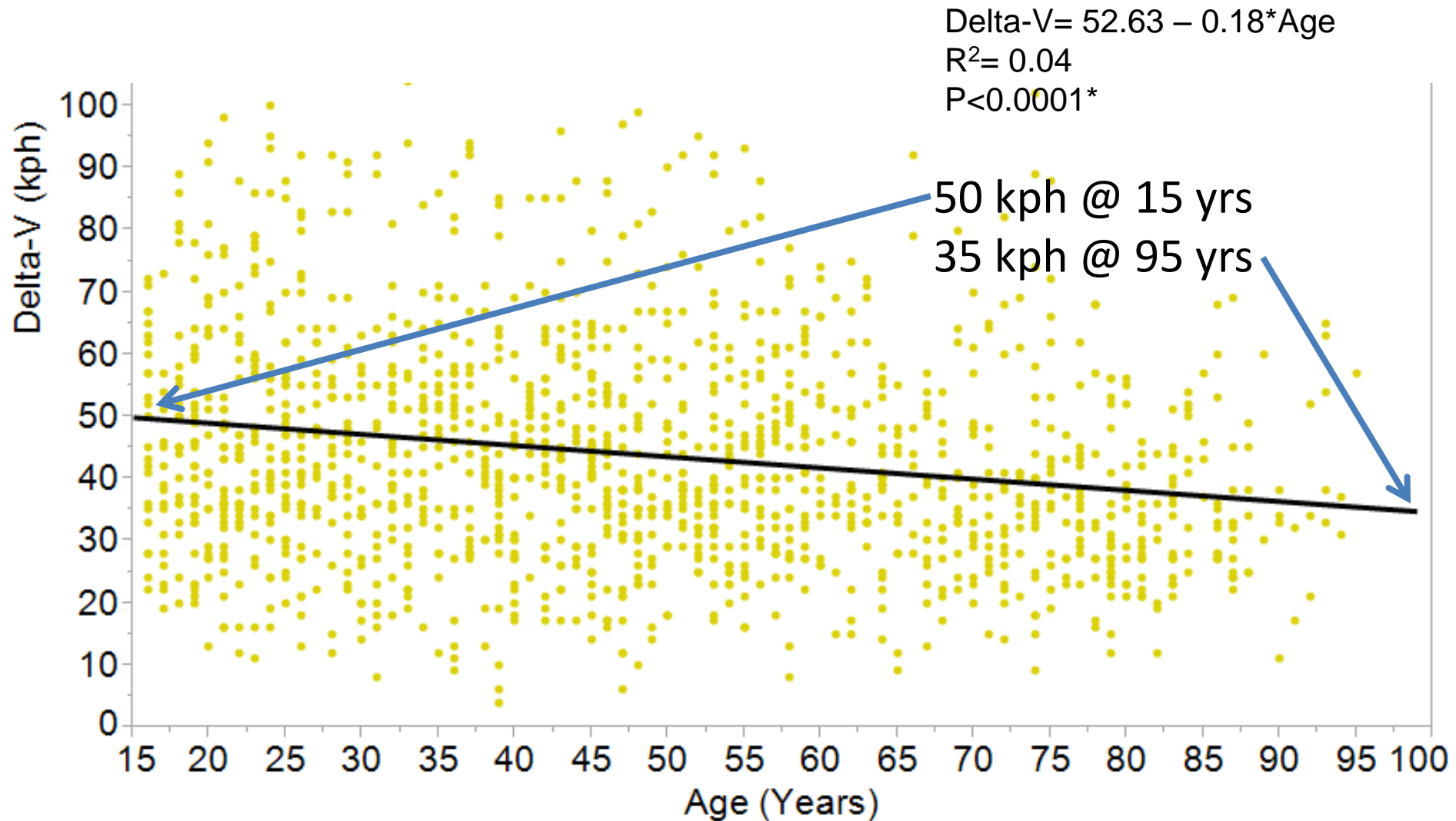
- 862 patients >59 years
- 2465 fractures
- All types inversely correlated with ΔV
 - Spine
 - Upper extremity
 - Pelvis/lower extremity
 - Thorax



NASS – All Body Regions, AIS 3+

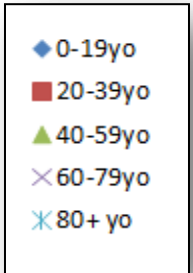


NASS, Thorax – AIS 3+

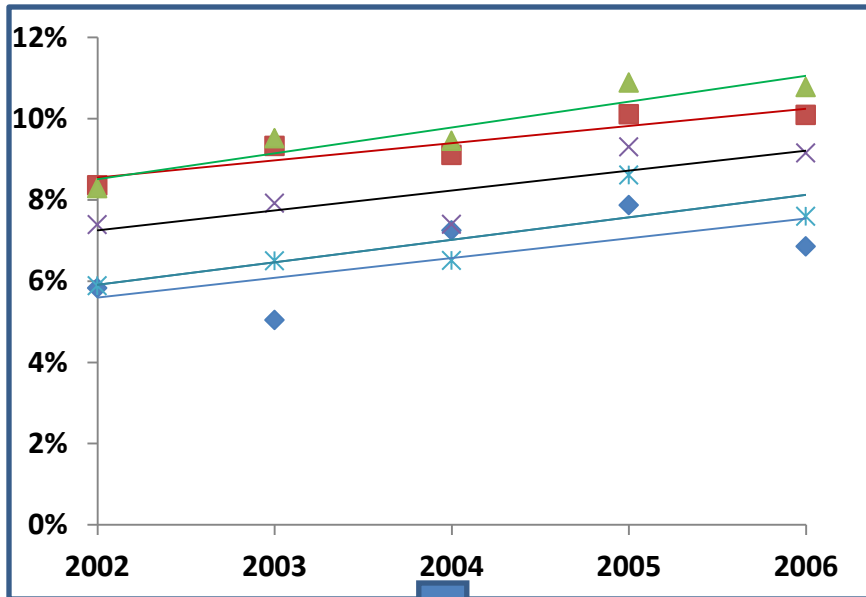


Incidence Rates of TL injuries in NTDB

$$\text{Incidence Rates} = \frac{\text{\# of MVC-Induced TL Injuries per age group per year}}{\text{Total \# of all MVC-Induced Injuries per age group per year}}$$

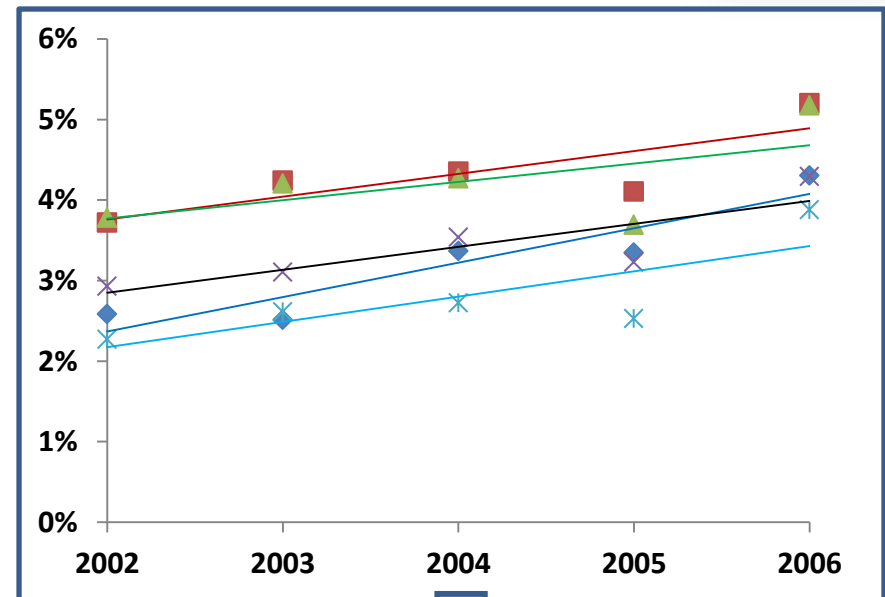


NTDB (AIS2+)



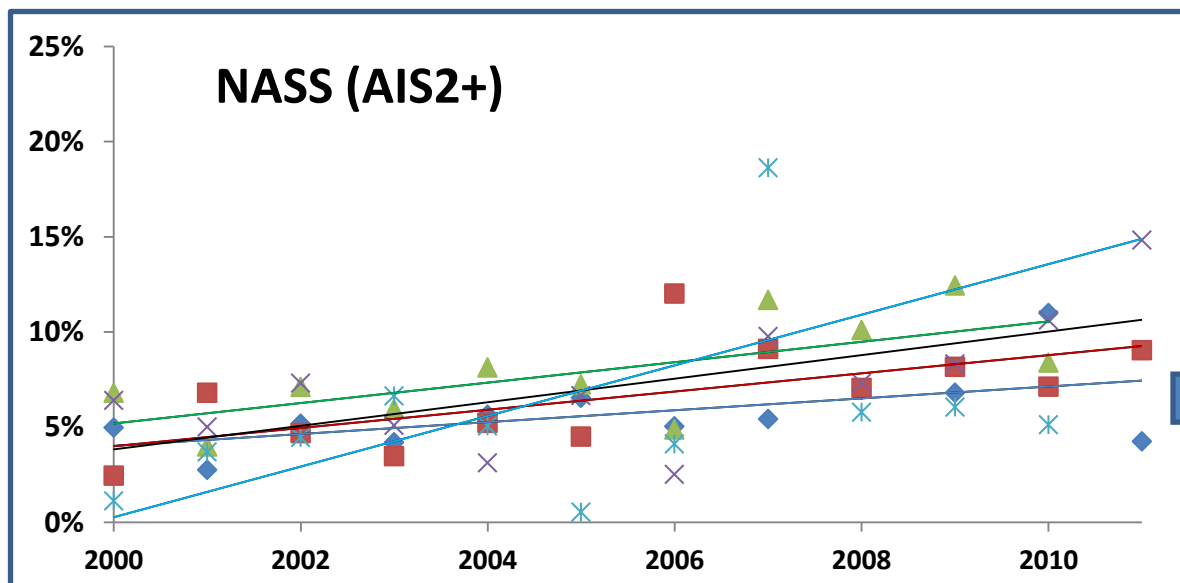
Age adjusted relative 8.22% annual increase =, $p < 0.0001$

NTDB (ICD9)



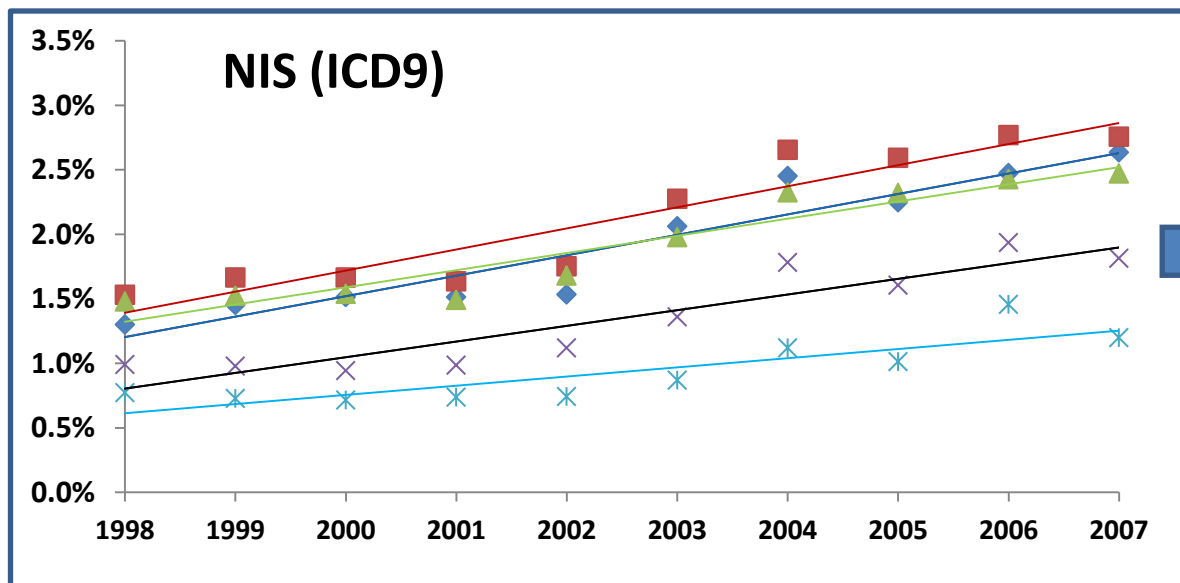
Age adjusted relative 8.59% annual increase, $p < 0.0001$

Incidence Rates of TL injuries in NASS & NIS



$$\text{Incidence Rates} = \frac{\text{\# of MVC-Induced TL Injuries per age group per year}}{\text{Total \# of all MVC-Induced Injuries per age group per year}}$$

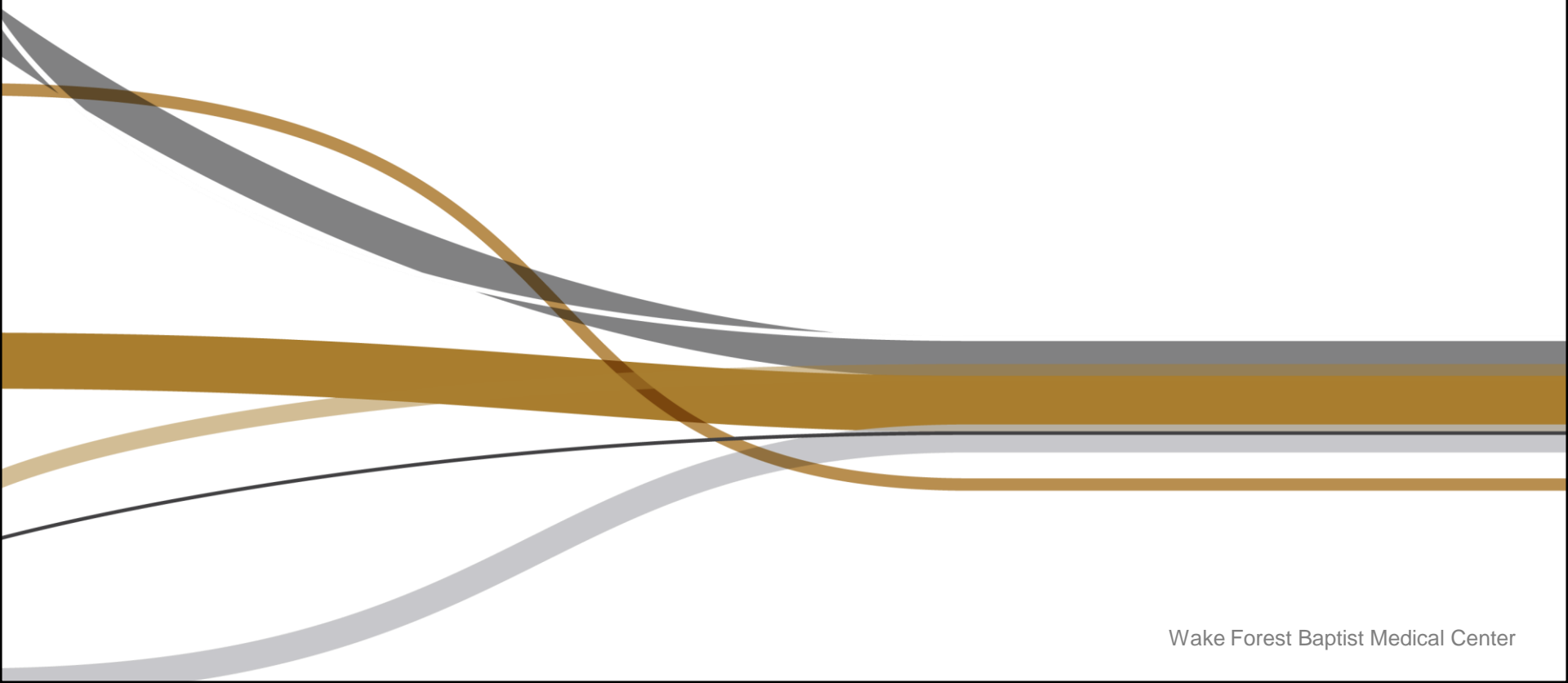
Age adjusted 8.10% annual increase, $p < 0.0001$



Age adjusted 8.12 % relative annual increase, $p < 0.0001$

Methods

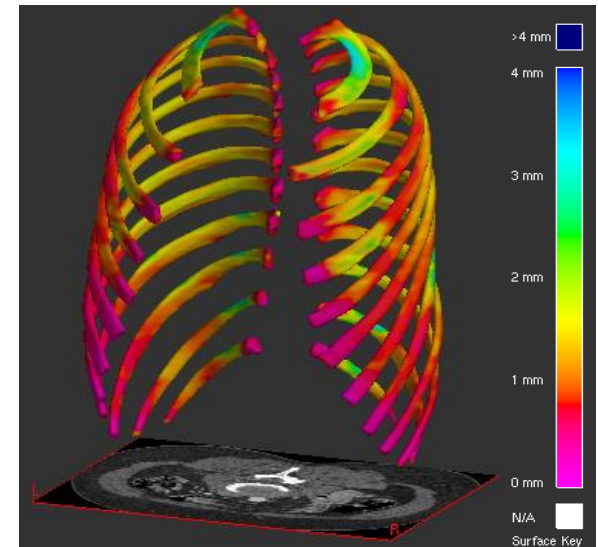
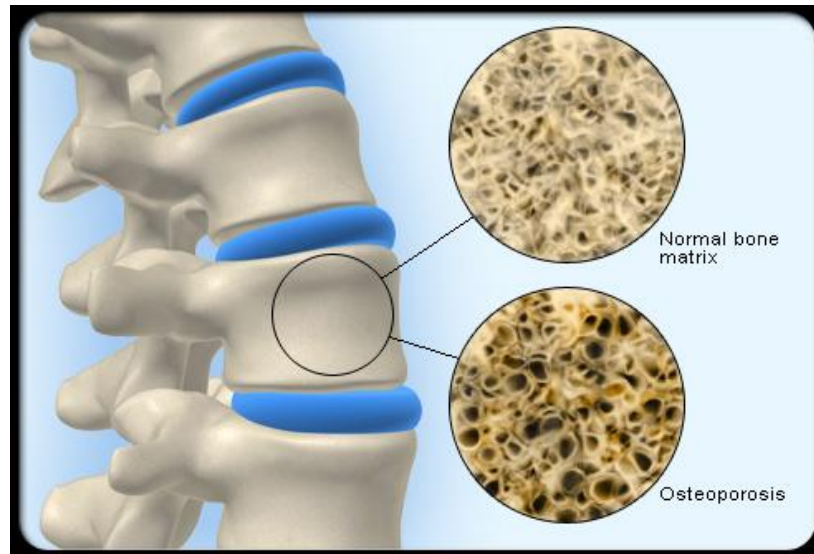
(Transition)



Bone Quality

An amalgamation of all factors that determine how well the skeleton can resist fracturing*

- Strength / fragility
- Thickness
- Biomarkers: osteoclasts, osteoblasts
- Density



Cortical Thickness Estimation (CT)

* Licata, A., *Bone Density vs Bone Quality: What's a Clinician to Do?* 2009

Bone Mineral Density (BMD)

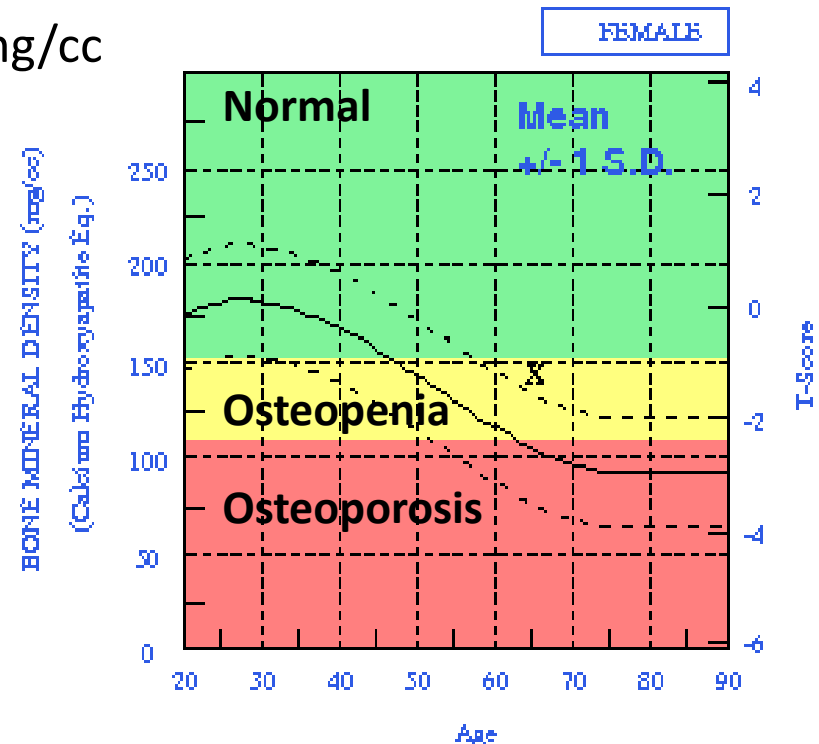
Amount of calcium & other minerals per bone area / volume

DXA Measures

- aBMD, Areal (g/cm^2)
- T-score = $(\text{aBMD}_{\text{Patient}} - \text{aBMD}_{\text{Reference}_{30\text{yo}}}) / \text{StDev}$
- Z-score = $\text{aBMD}_{\text{Patient}} - \text{aBMD}_{\text{Reference}(\text{age, sex, race, and/or skeletal site})}$

CT Measures

- vBMD, Volumetric (mg/cc) – calcium hydroxyapatite reference
- Hounsfield Units (HU) – correlated w/ mg/cc



Hounsfield Unit

- Houndsfield
 - Hounds in a field?



- Houndsfeld

– Hounds feld? Hounds in a german field?



- Hounsfield
 - Houns feld?

- Hounsfield
 - Houns in a field



Neuschwanstein
Outside Munich



Hounsfield Unit Range



Air: -1024 to -1000



Water: 0



Blood: 30 to 100



Bone: 1000

Lowest
Possible
Value:
-1024

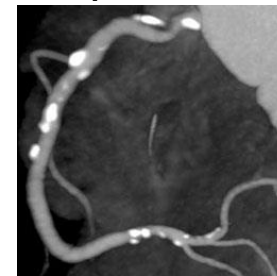


Fat: -120 to -50



Muscle: 10 to 40

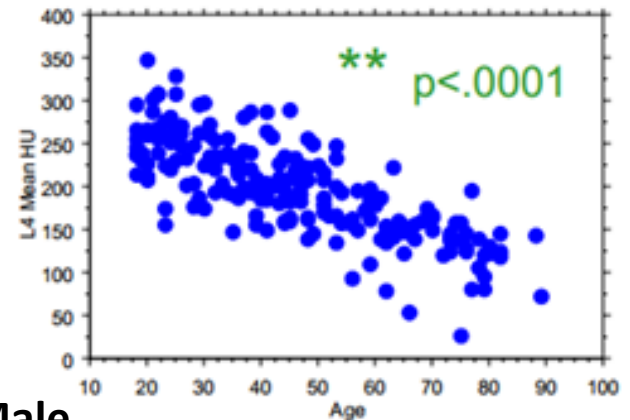
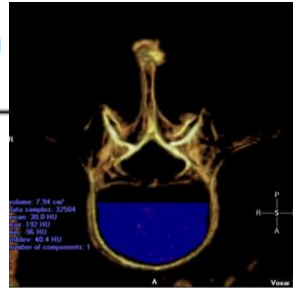
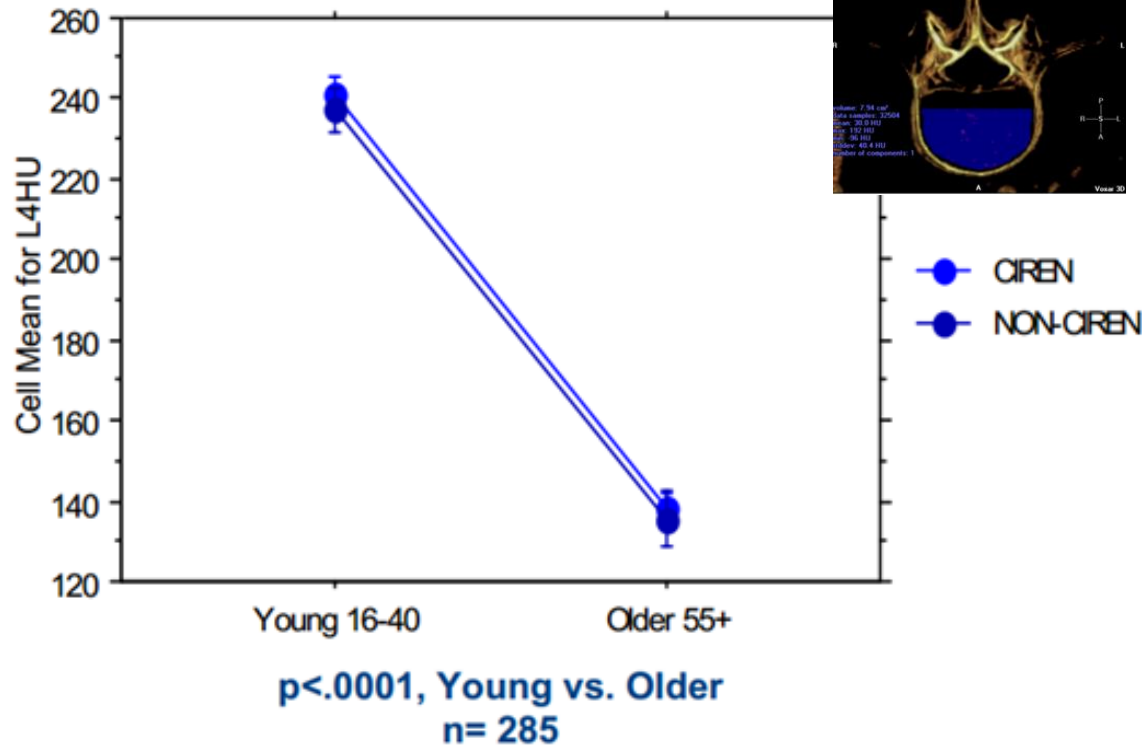
Calcified
Plaques: 130



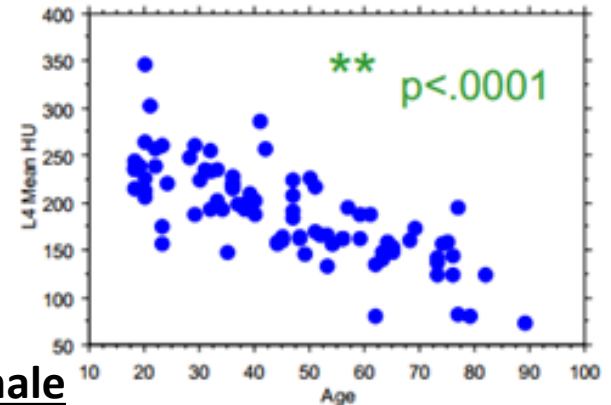
Highest
Possible
Value:
3071

Previous CIREN BMD Research

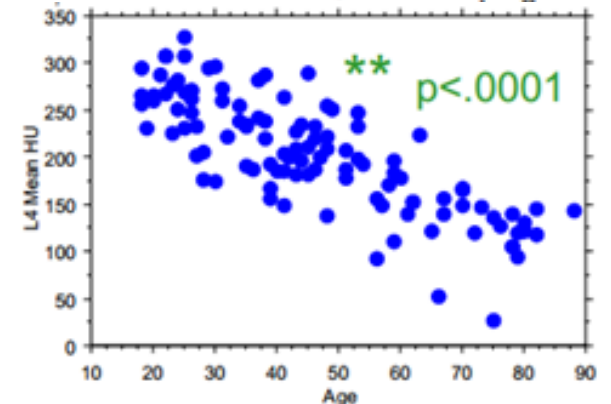
Bone Mineralization (L4HU)



Male

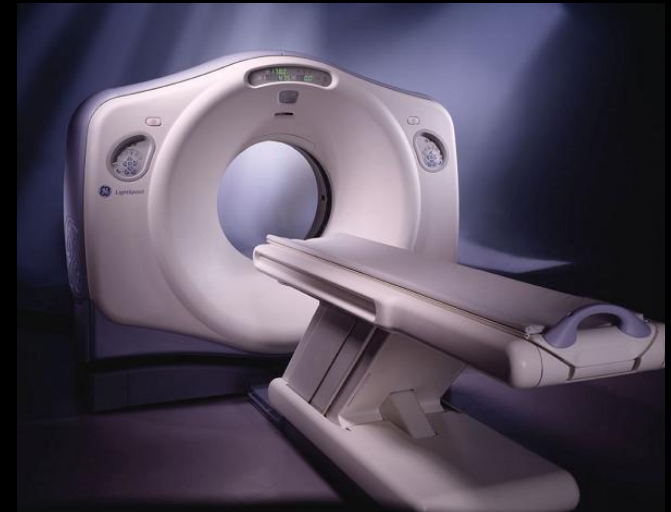
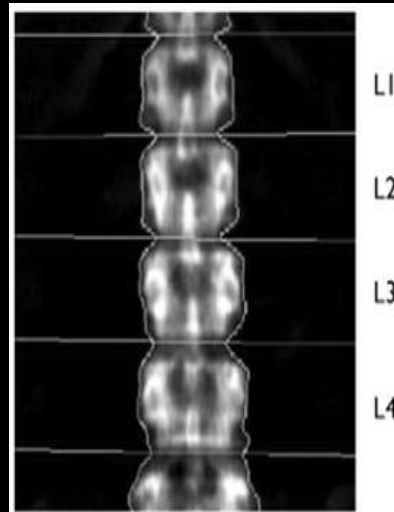


Female



- Bone loses density in males & females
- L4HU is significantly associated with increased number of rib fractures

Dual-energy X-ray Absorptiometry (DXA) vs Computed Tomography



Most widely recognized BMD test to determine bone health

Identifies osteoporosis, fracture risk, and measures response to osteoporosis treatment

aBMD, T-scores to diagnose osteopenia/porosis

QCT – phantom-based BMD estimation

All CIREN patients typically get: abdominal CT with no phantom

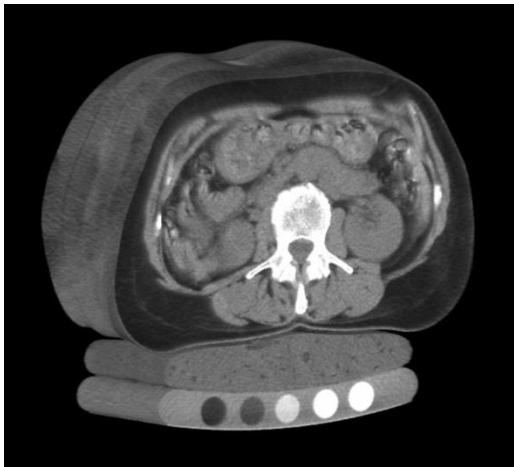
vBMD (mg/cc), HU measures

Goal: Measure vBMD of lumbar spine in CIREN patients from phantom-less abdominal CT

CIREN BMD Analysis Workflow

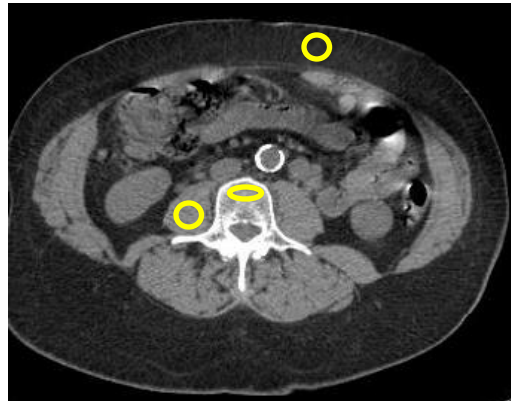
Validate Phantom-less
Calibration Methods

CLIP II pilot data:
DXA & QCT Measures



Quantify BMD in
CIREN Occupants

Collect BMD & tissue
measures for calibration

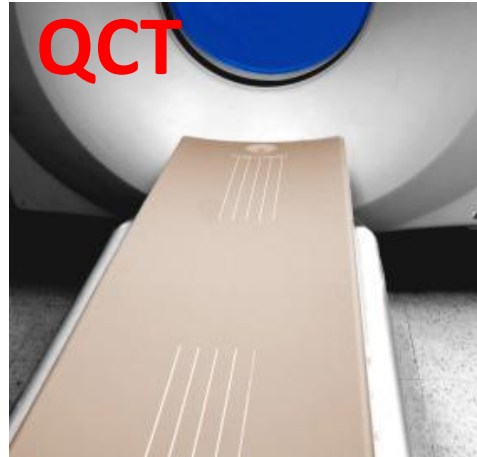
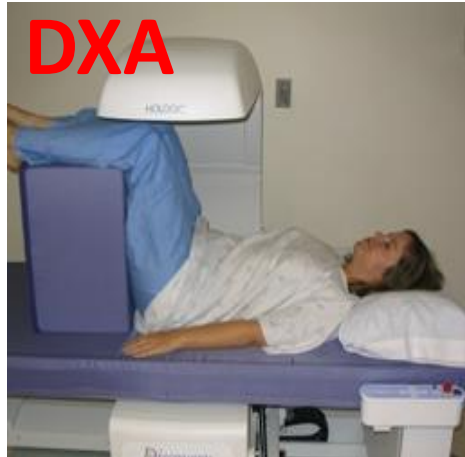


Correlate BMD with
CIREN Data

Relate BMD to CIREN
occupant demographics,
comorbidities, injuries



Cooperative Lifestyle Intervention Program (CLIP II) Bone Study



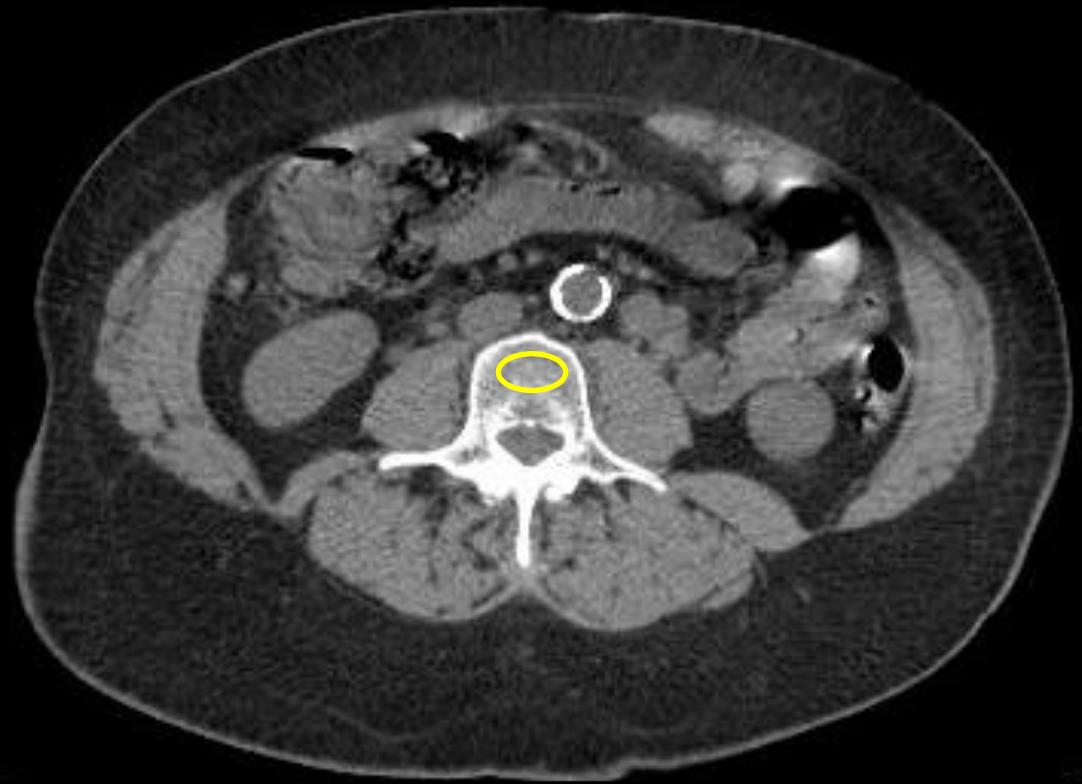
- Study of effect of exercise modality during weight loss on bone density & quality
- Paired lumbar aBMD (DXA) & vBMD (QCT) in 50 subjects

CLIP II Study Population				
Characteristic		M (n = 17) Mean \pm SD	F (n = 33) Mean \pm SD	Overall (n = 50) Mean \pm SD
Age (years)		65 \pm 5	66 \pm 4	66 \pm 4
Weight (kg)		109 \pm 16	89 \pm 12	96 \pm 16
BMI (kg/m ²)		34 \pm 4	34 \pm 4	34 \pm 4
L1-L4 DXA	<i>Normal</i>	14	28	42
T-score	<i>Osteopenia</i>	3	5	8
(# subjects)	<i>Osteoporosis</i>	1	0	1

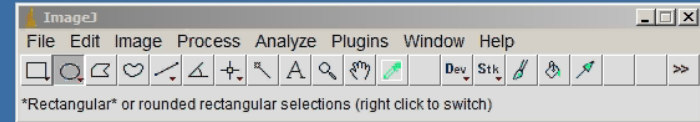
Lumbar Spine BMD Analysis of CT Scans

- CLIP II & CIREN abdominal CT scans analyzed
- Mean HU within ROIs at L1-L5 vertebrae

	Area	Mean	Min	Max
1	308.990	133.460	18	225
2	308.990	129.380	37	227
3	308.990	120.386	35	230
4	308.990	132.457	29	238
5	308.990	122.370	17	225



Lumbar Spine BMD Analysis of CLIP II & CIREN CT Scans with ImageJ



CLIP11: ROIs for ImageJ Calibration to mg/cc

Calibration Measurements

ROIs at the location of L4 vertebra

Port 1: fat equivalent

Port 2: 0 mg/cc CaHA

Port 3: 75 mg/cc CaHA

Port 4: 150 mg/cc CaHA

Muscle: right psoas

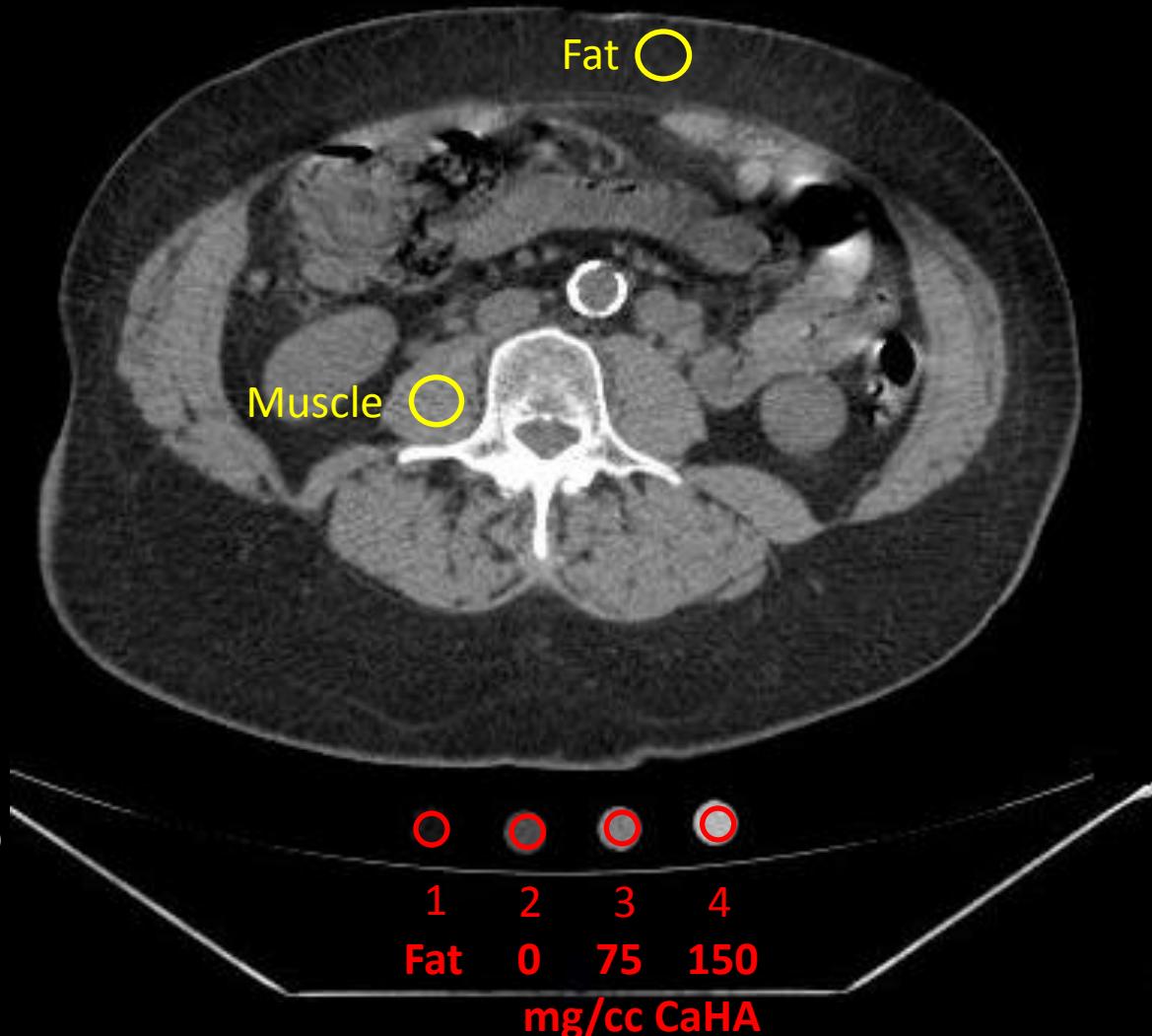
Fat: subcutaneous, anterior

Phantom calibration technique

Ports 2-4: Phantom port measurements used to calibrate;

Fat-muscle calibration technique

Muscle & Fat ROI measures used to calibrate



INTable Calibration Phantom

http://www.image-analysis.com/intable_phantom

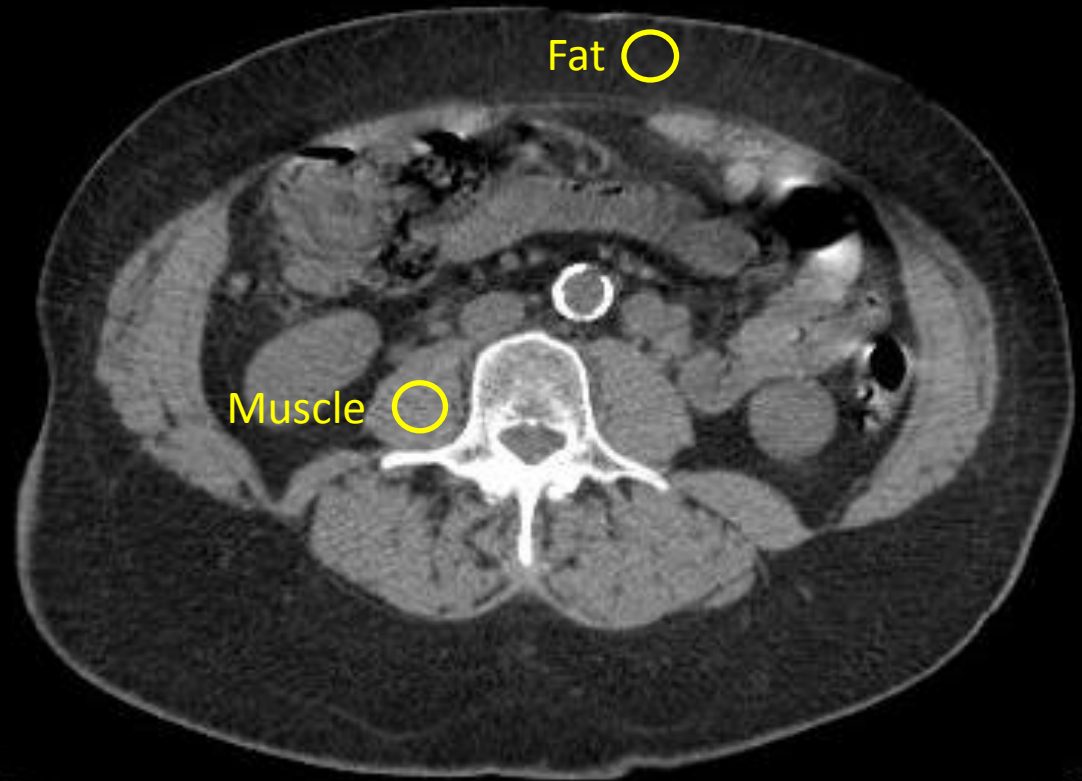
CIREN: ROIs for ImageJ Calibration to mg/cc

Calibration Measurements

ROIs at the location of L4 vertebrae

Muscle: right psoas

Fat: subcutaneous, anterior



Fat-muscle calibration technique

Muscle & Fat ROI measures used to calibrate



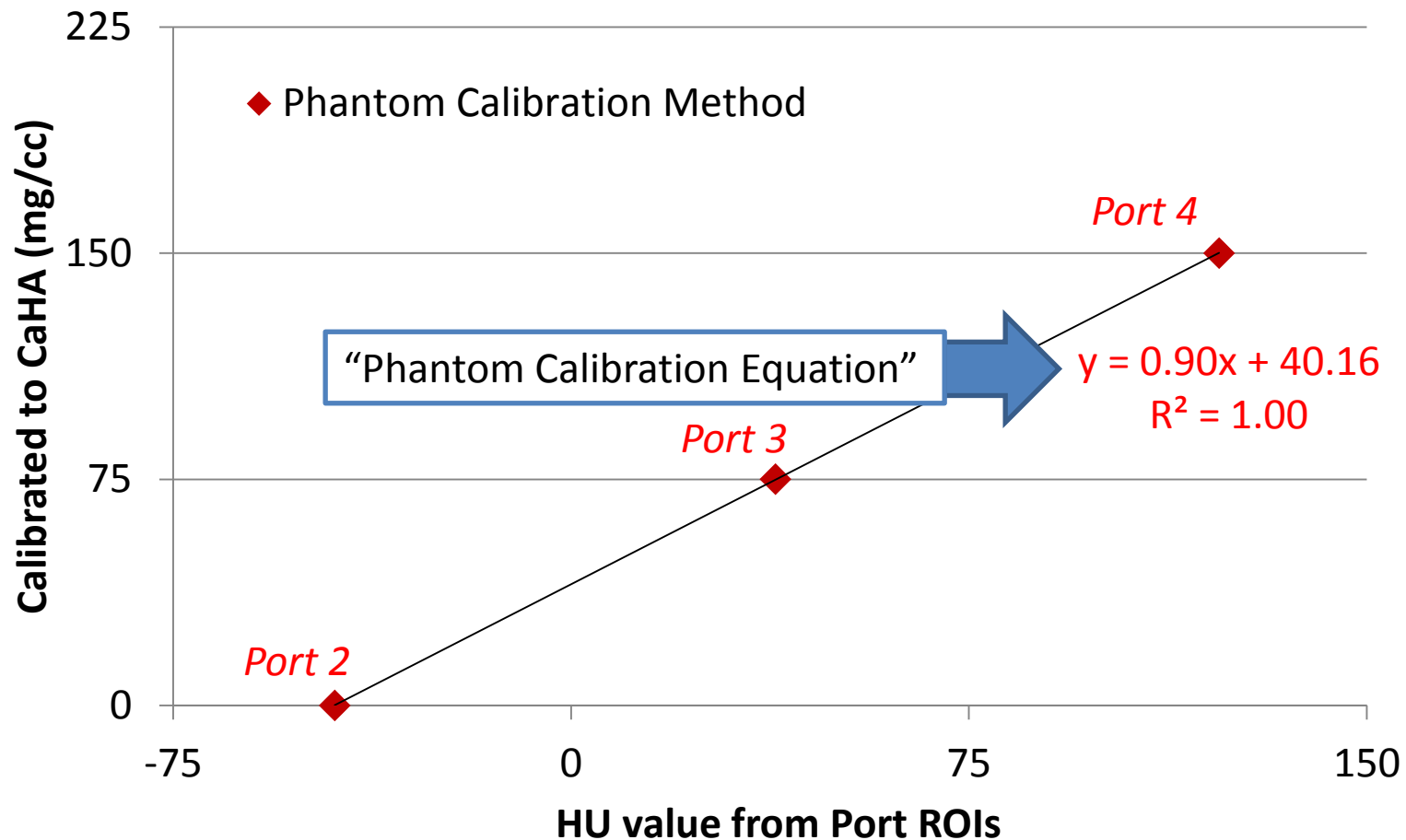
Fat 0 75 150
mg/cc CaHA

Phantom Calibration Method

Phantom calibration technique applied to each CLIP II subject scan:

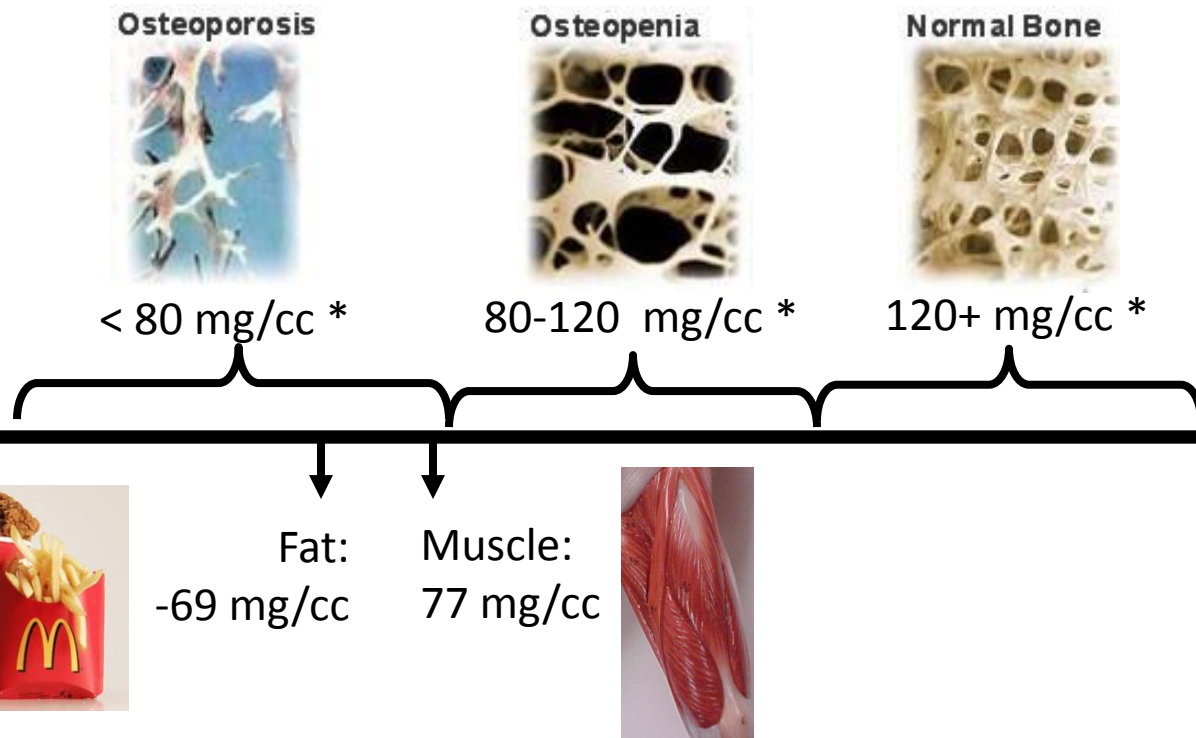
Linear regression fit:

[0, 75, 150] mg/cc CaHA *versus* Ports 2-4 ROI measures



Phantom Calibration Equation

- “Phantom Calibration Equation” for each CLIP II subject used to calibrate ROI measures of:
 - L1-L5 vertebrae, fat, muscle
- Fat & Muscle “Assumed ground truth values” computed from mean of calibrated ROIs of all CLIP II subjects

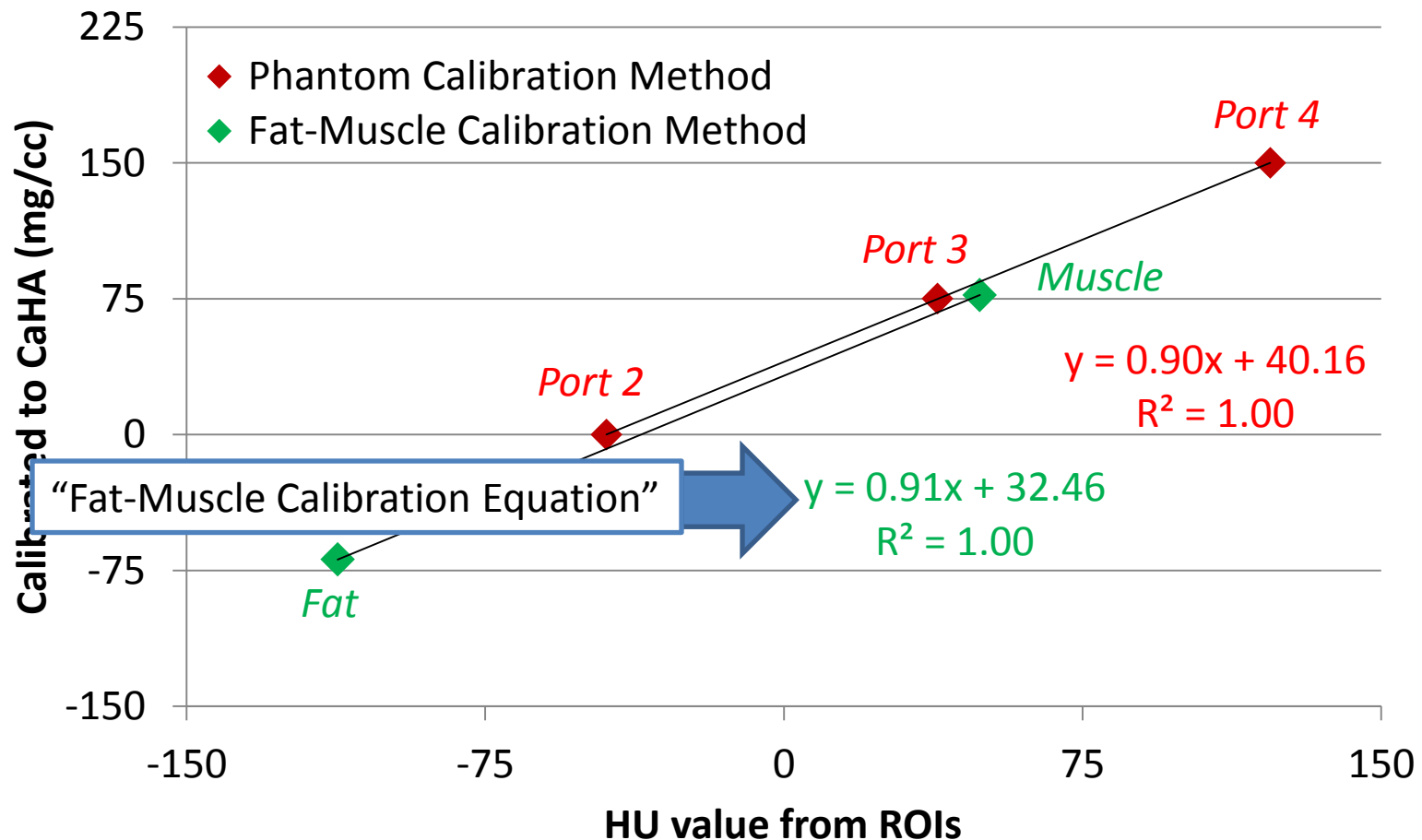


Fat-Muscle Calibration Method

Fat-muscle calibration technique applied to each CLIPII subject scan:

Assumed ground truth values: Fat = -69, Muscle = 77 mg/cc CaHA

Linear regression fit: [-69 77] mg/cc CaHA vs [Fat Muscle] ROI measures

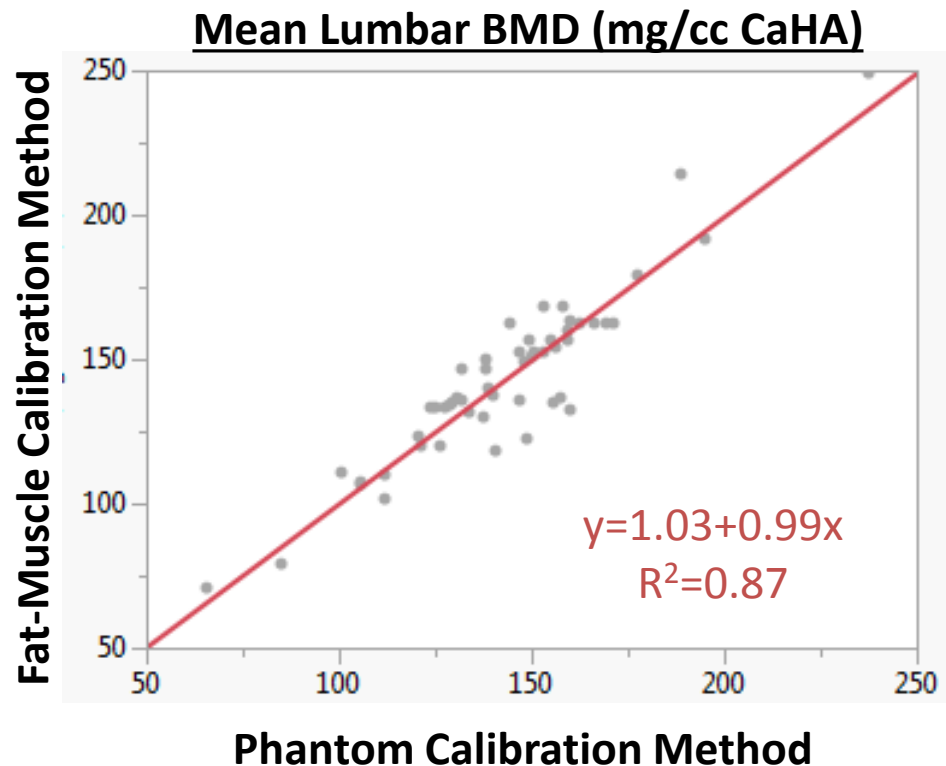


Fat-Muscle Calibration Equation

- “Fat-Muscle Calibration Equation” for each CLIPII subject used calibrate ROI measures of:
 - L1-L5 vertebrae
- Mean Lumbar BMD of L1-L5 vertebrae measures computed using:
 - Phantom Calibration Method
 - Fat-Muscle Calibration Method

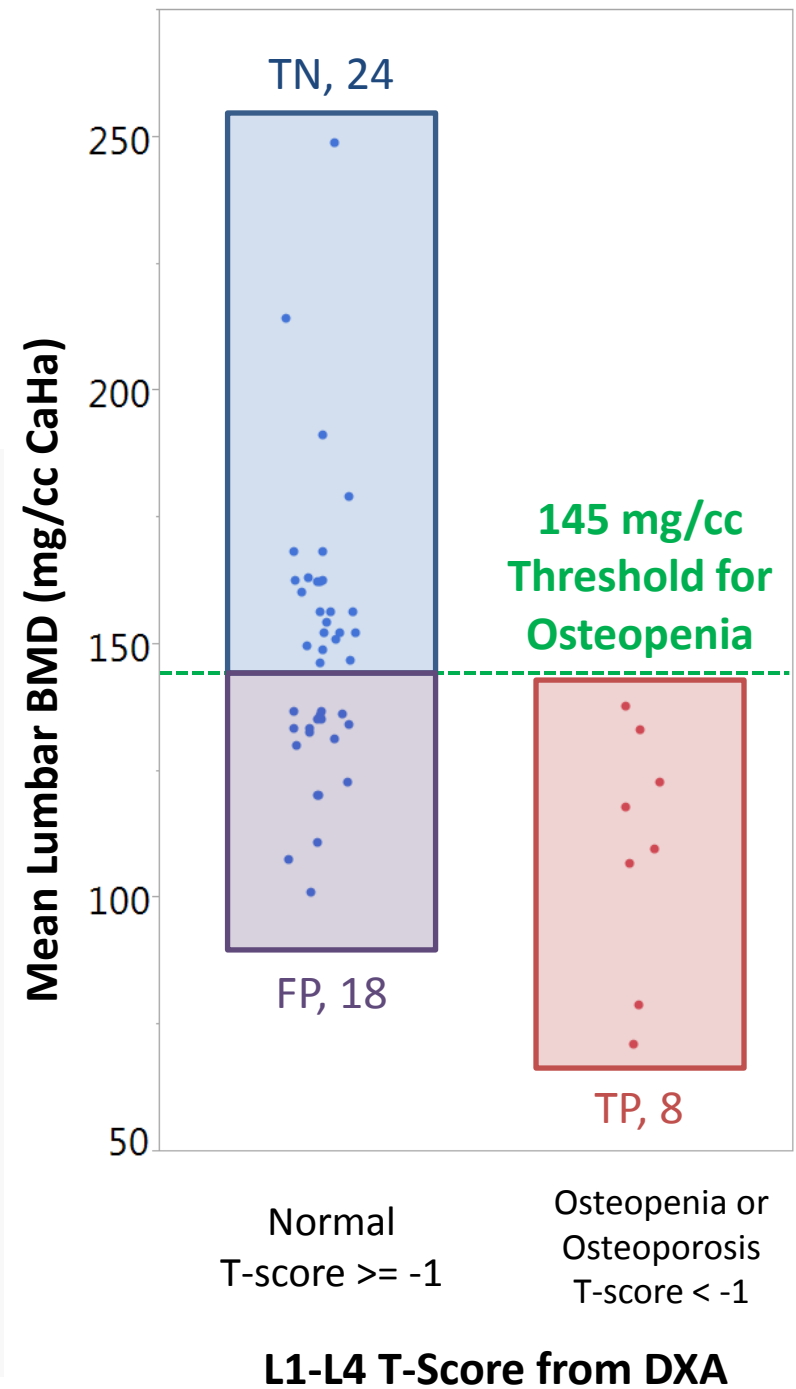
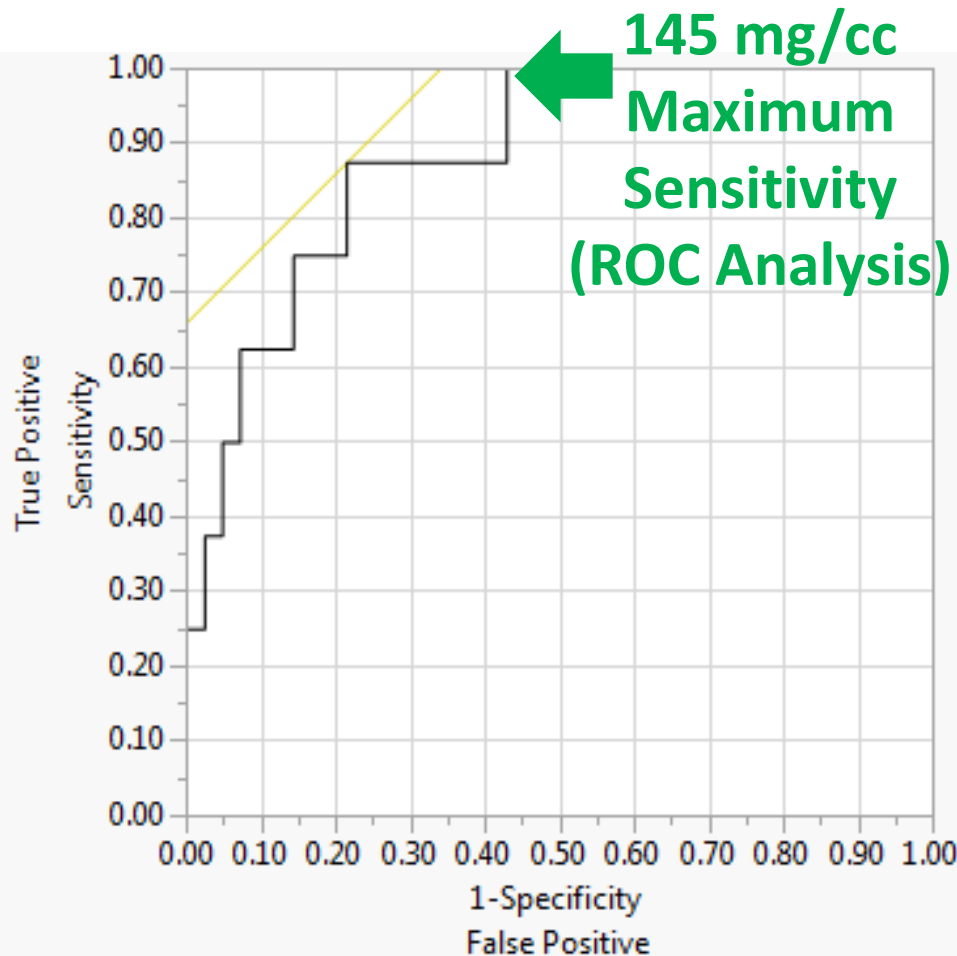
Summary:

1. Fat-Muscle calibration method replicates phantom calibration method well
2. Method applied to phantom-less CIREN scans



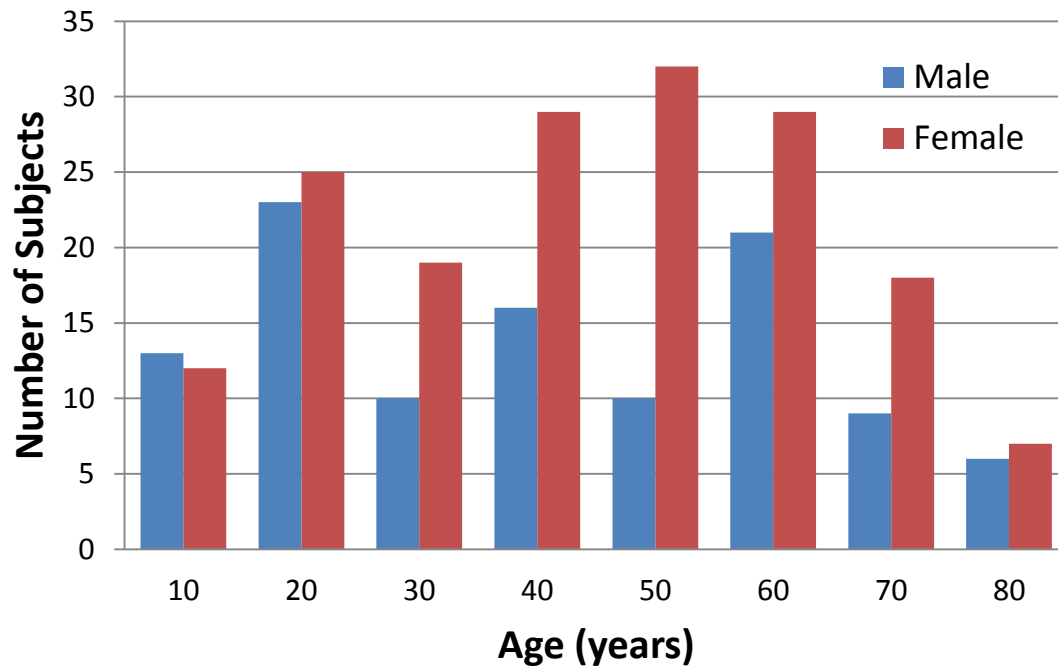
CT-based Predictive mg/cc Threshold for Osteopenia

- DXA/CT, 50 CLIP-II subjects



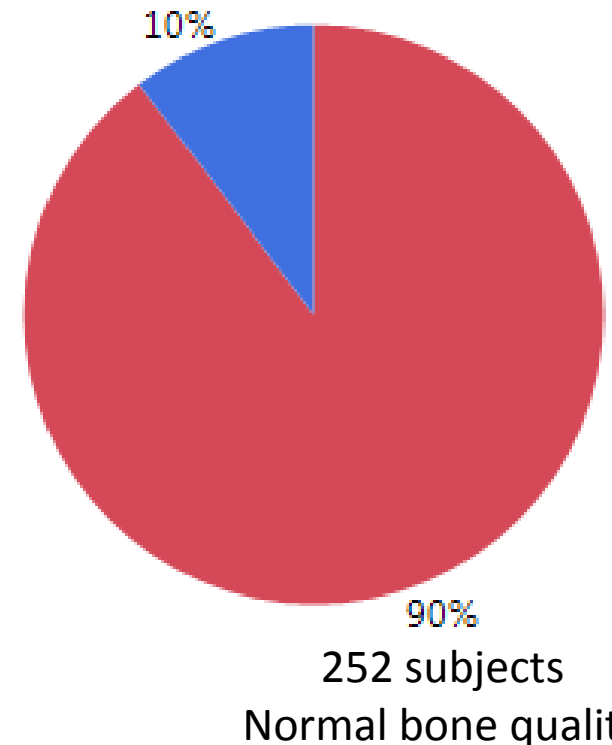
CIREN Study Population

- CIREN Inclusion criteria: WFU cases, Ages 16+, abdominal CT, no hardware in scan
- 281 subjects (109 M, 172 F)

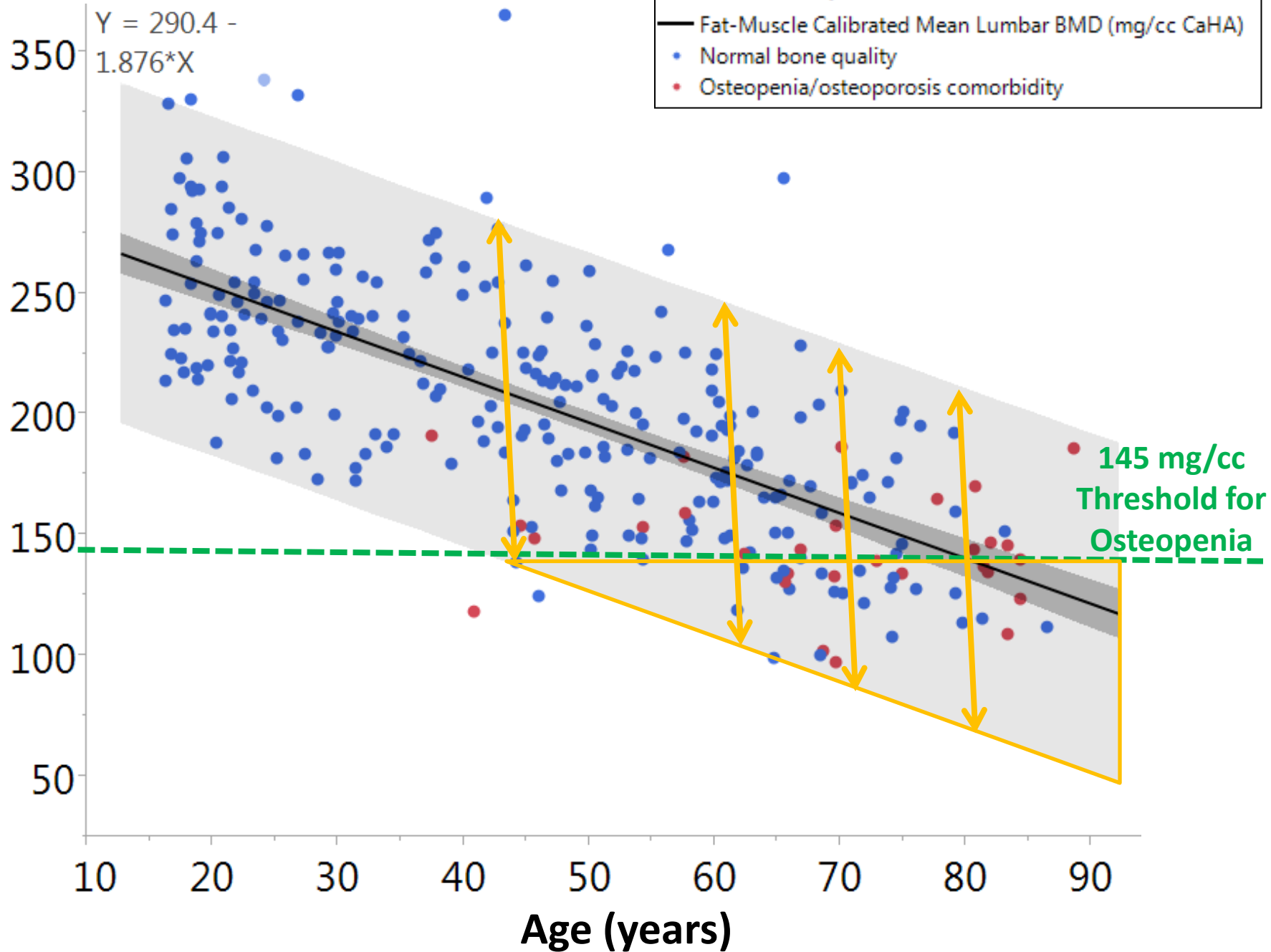


CIREN Comorbidities

Osteopenia/Osteoporosis
29 subjects



Mean Lumbar BMD (mg/cc CaHA)



Mean Lumbar BMD (mg/cc CaHA)

350
300
250
200
150
100
50

10 20 30 40 50 60 70 80 90

Age (years)

$$Y = 290.4 - 1.876 * X$$

CIREN Comorbidity

— Fat-Muscle Calibrated Mean Lumbar BMD (mg/cc CaHA)

• Normal bone quality

• Osteopenia/osteoporosis comorbidity

65F, Offset frontal, multiple impacts, Fxs:
R ribs 7-10, L rights 1-5, 12, pelvis,
humerus, L5 transverse process, scapula

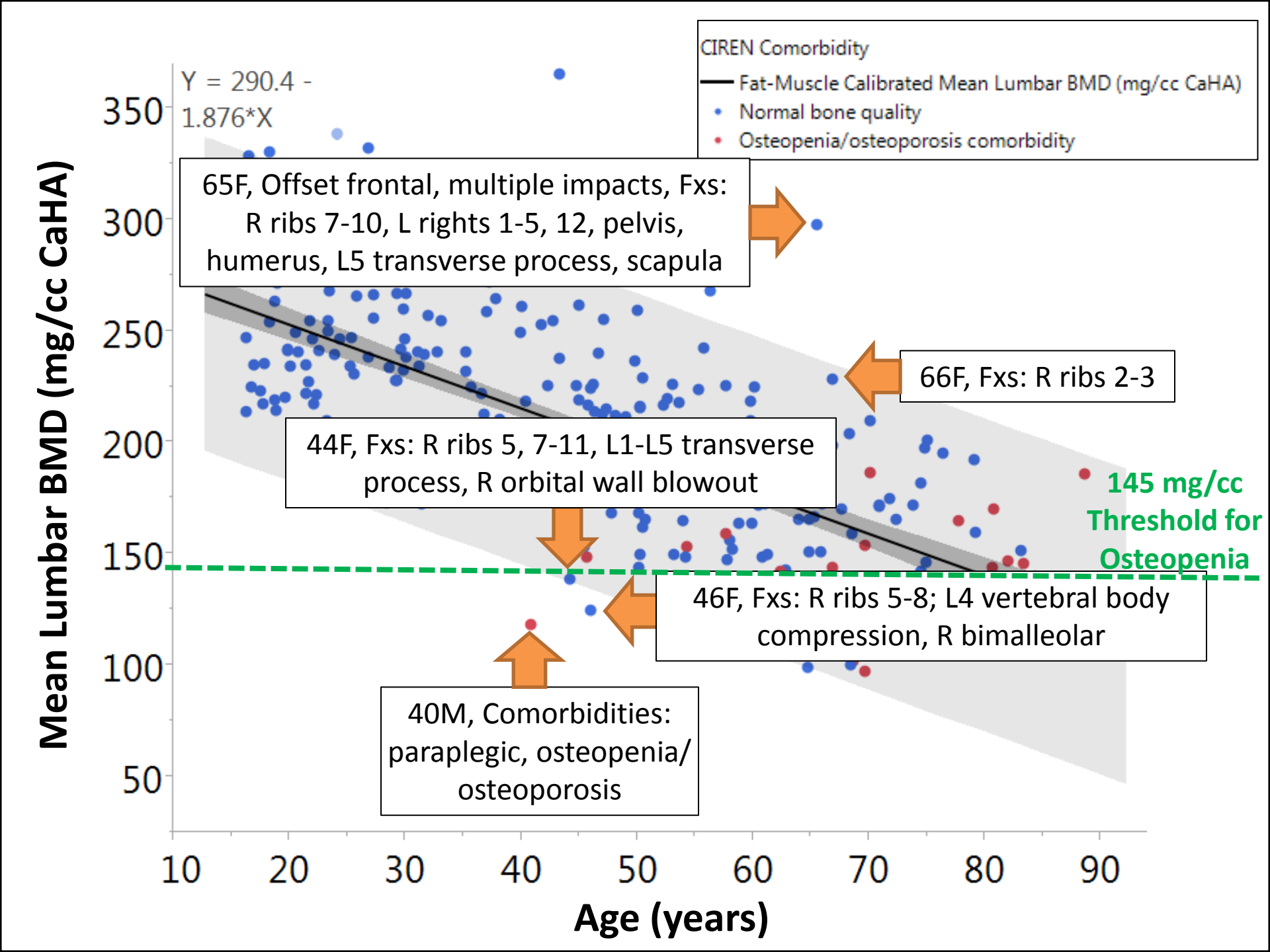
66F, Fxs: R ribs 2-3

44F, Fxs: R ribs 5, 7-11, L1-L5 transverse
process, R orbital wall blowout

145 mg/cc
Threshold for
Osteopenia

46F, Fxs: R ribs 5-8; L4 vertebral body
compression, R bimalleolar

40M, Comorbidities:
paraplegic, osteopenia/
osteoporosis



Mean Lumbar BMD (mg/cc CaHA)

$$Y = 290.4 - 1.876 * X$$

- Normal ≥ 145 mg/cc
- Osteopenia < 145 mg/cc
- Fat-Muscle Calibrated Mean Lumbar BMD (mg/cc CaHA)

350

300

250

200

150

100

50

10

20

30

40

50

60

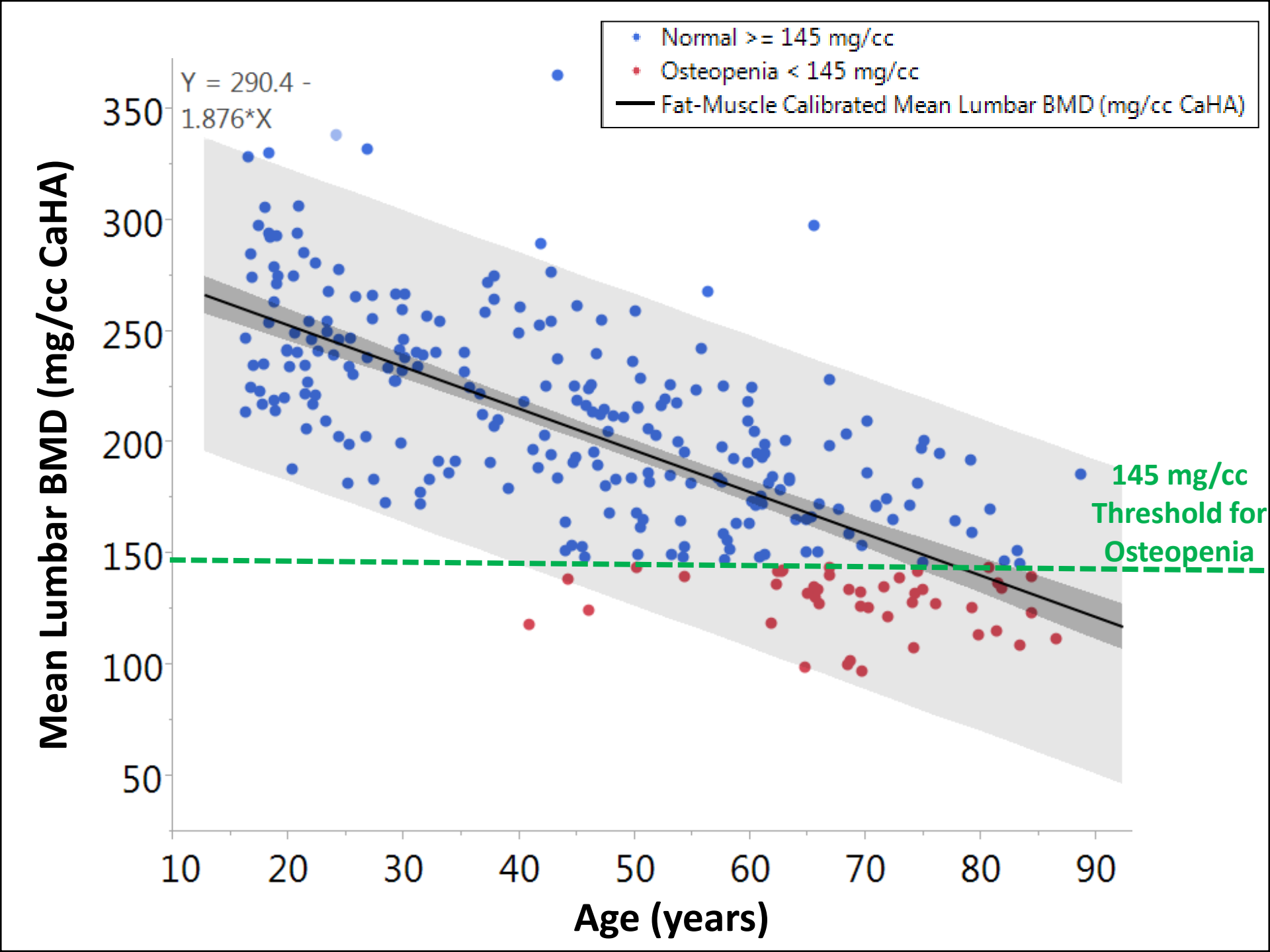
70

80

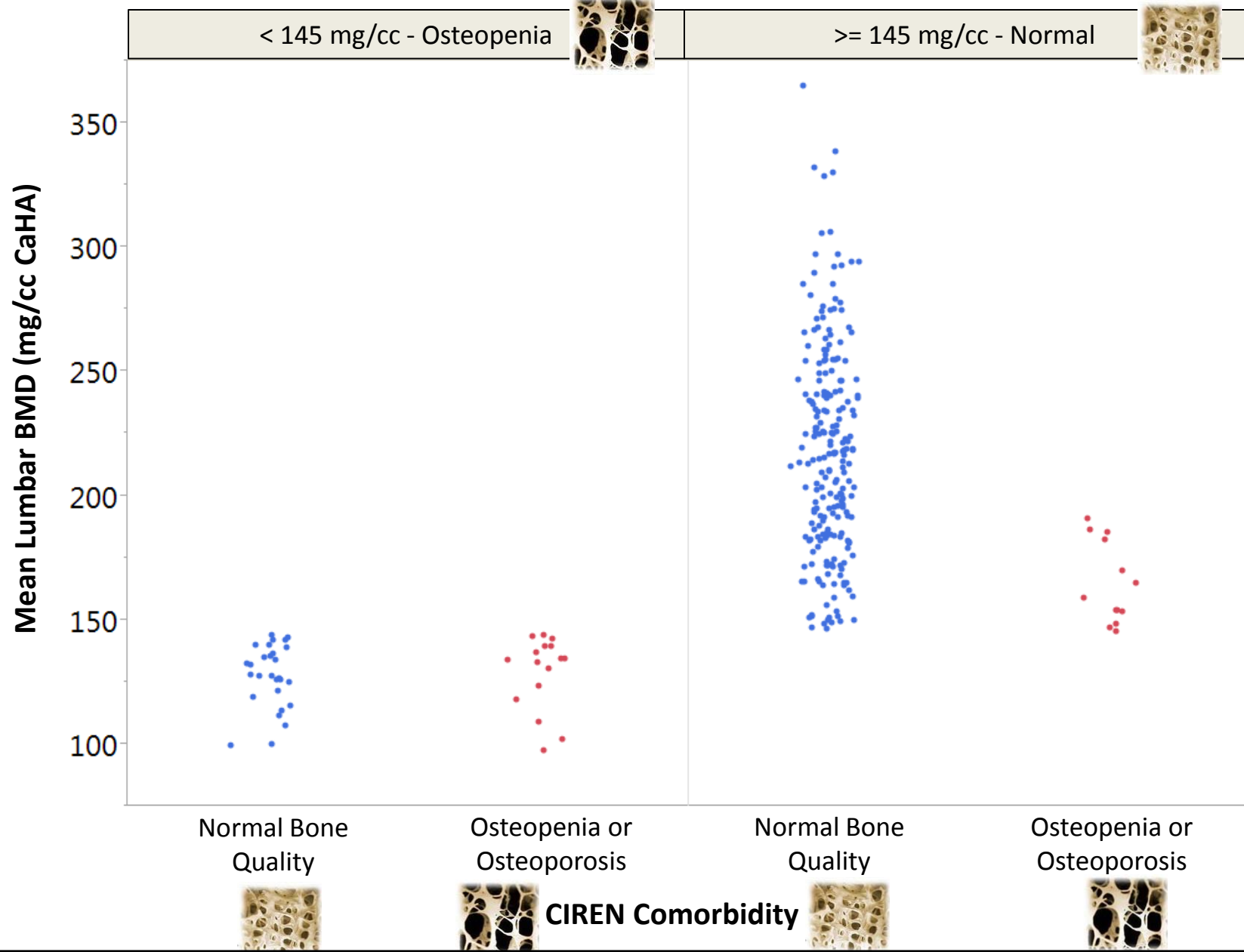
90

Age (years)

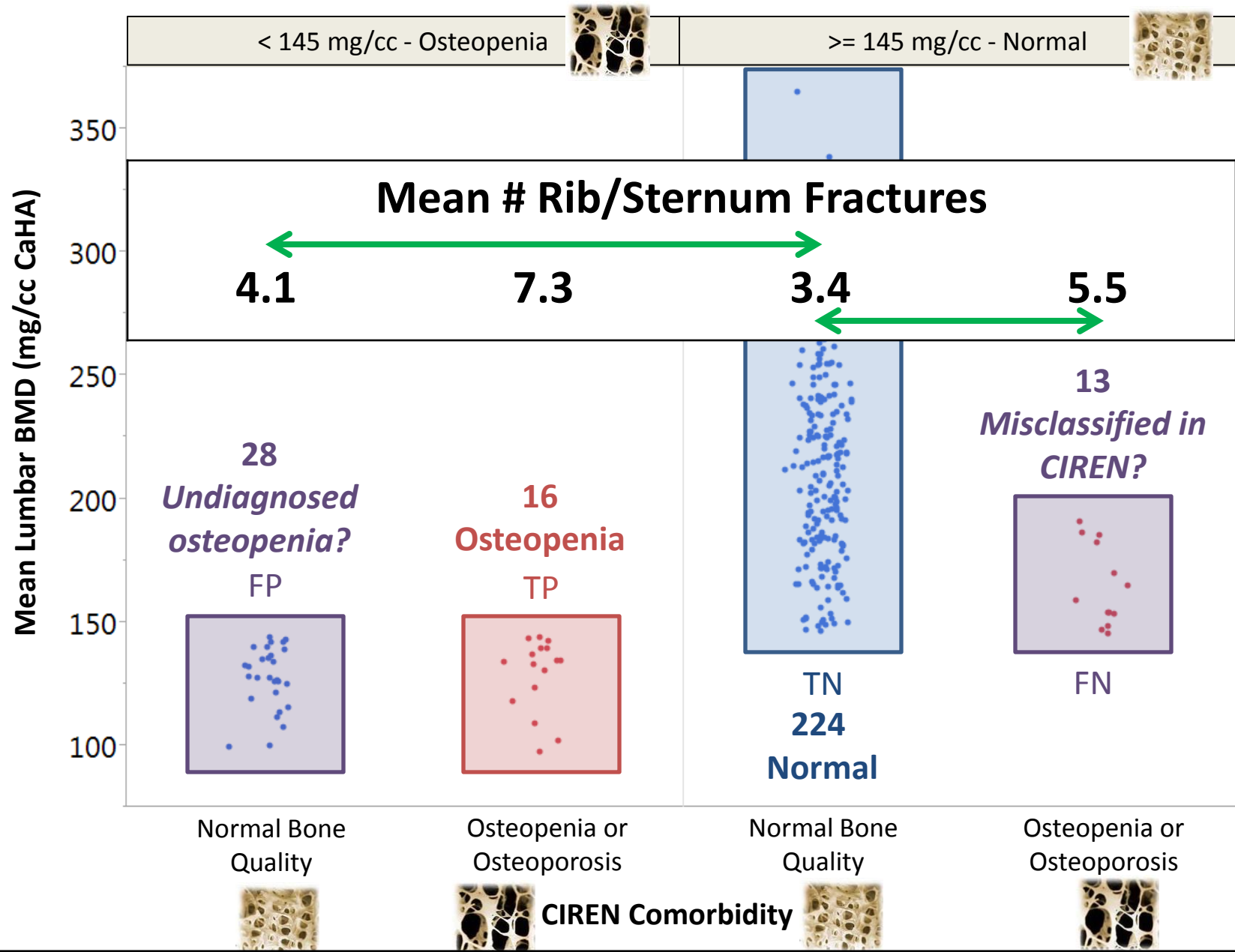
145 mg/cc
Threshold for
Osteopenia



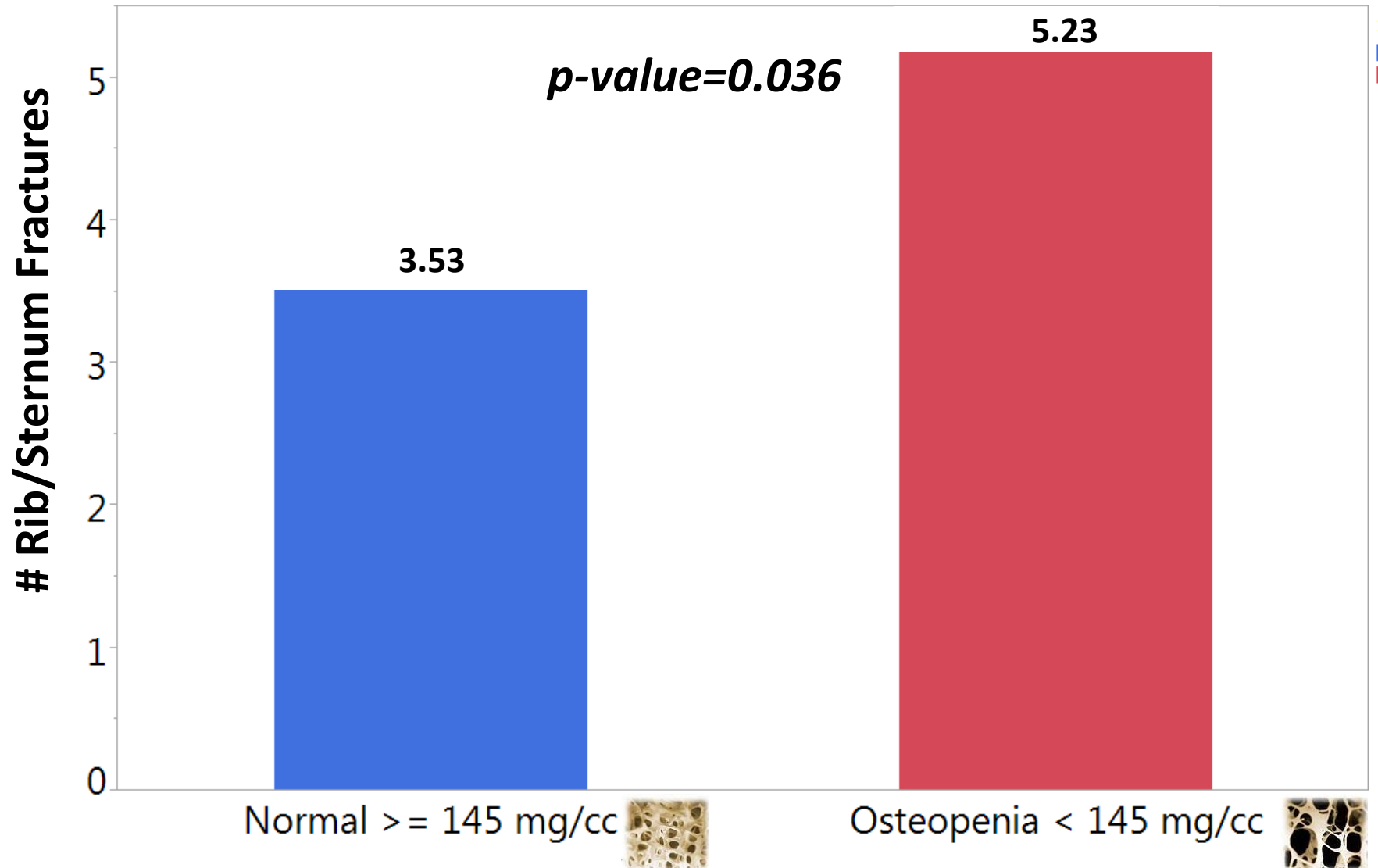
CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



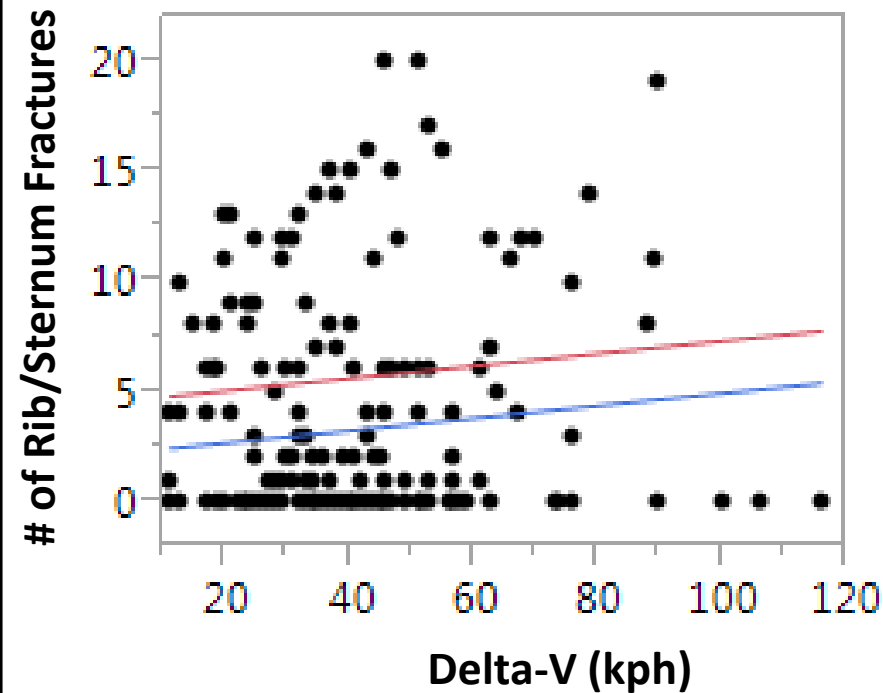
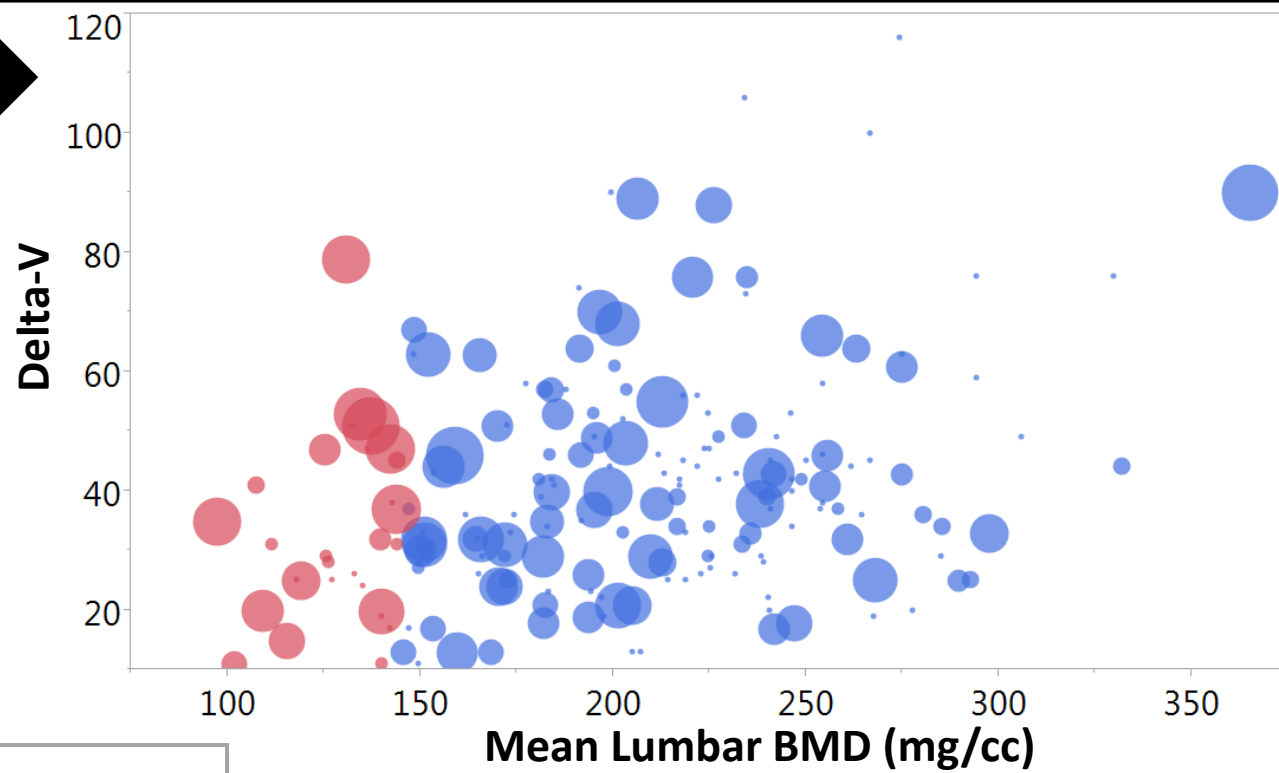
CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



Significantly Higher # Rib/Sternum Fractures in CIREN Occupants with vBMD < 145 mg/cc



Bubble Size:
Rib/Sternum Fxs



$p=0.038$

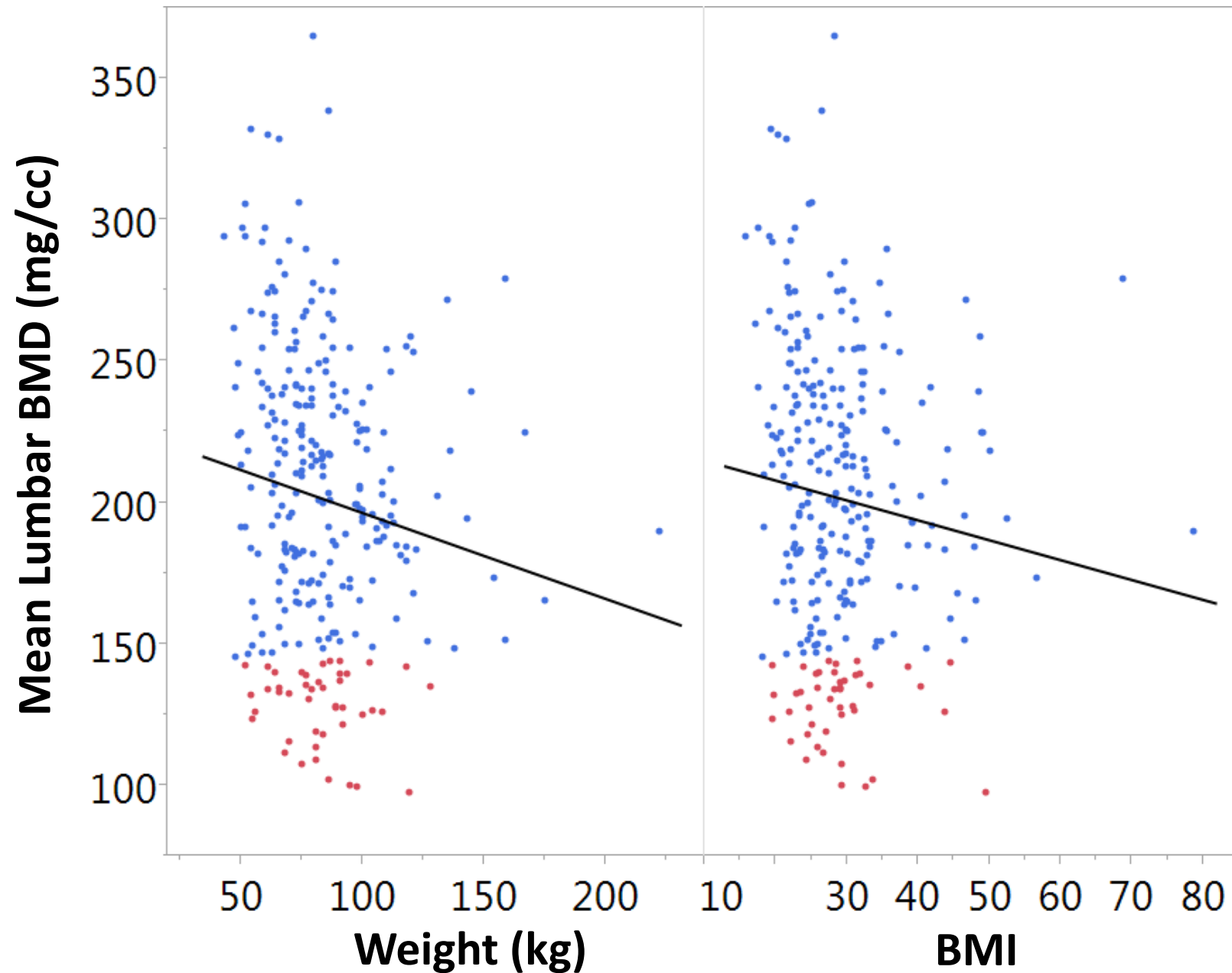
$$\# \text{ Rib/Sternum Fxs} = 3.33 + 0.03DV + 1.18BMD_{145}$$

— < 145 mg/cc

— ≥ 145 mg/cc

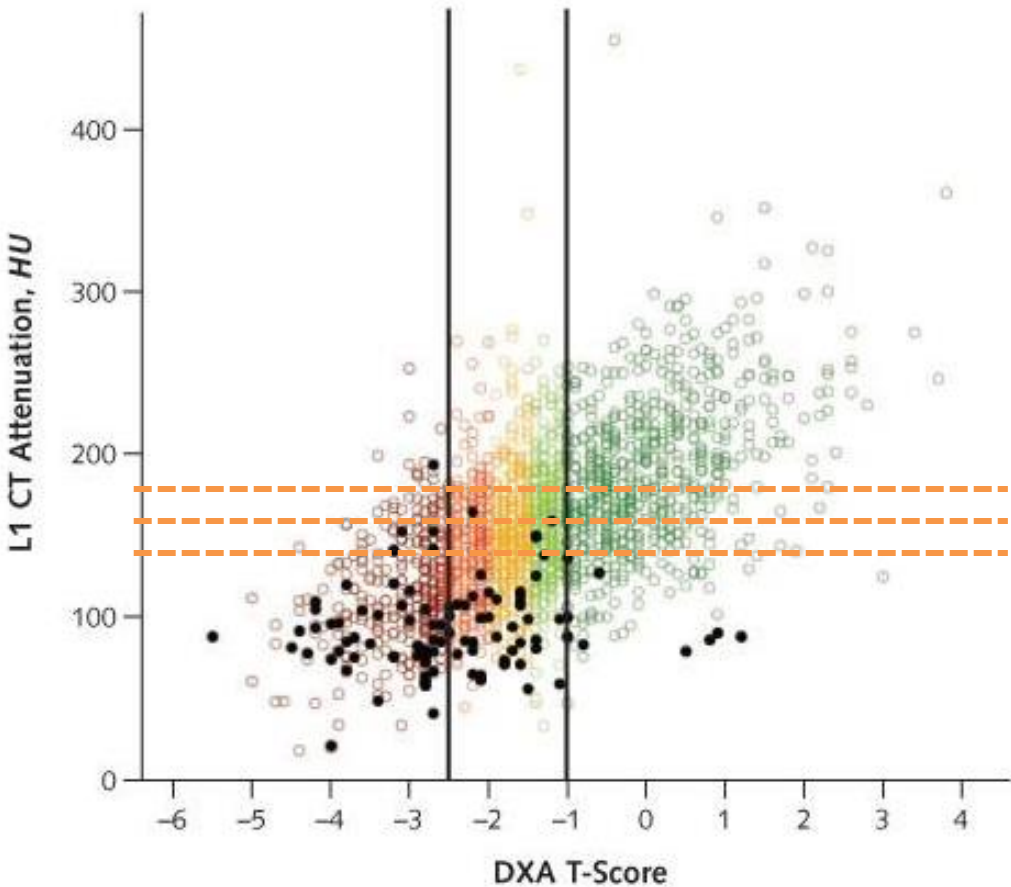
Higher Weight/BMI, Higher BMD?

• Normal ≥ 145 mg/cc
• Osteopenia < 145 mg/cc



Osteopenia Thresholds

Study	Mg/cc
American College of Radiology	120 mg/cc
Current Study (CIREN/CLIPII)	145 mg/cc
Pickhardt (2013), high sensitivity	135 HU
Image Analysis software	150 mg/cc
Pickhardt (2013), balanced sens./spec.	160 HU
Pickhardt (2013), high specificity	190 HU



- Normal (T-score ≥ -1)
- Mild osteopenia (-1.5 < T-score < -1)
- Moderate osteopenia (-2 < T-score ≤ -1.5)
- Advanced osteopenia (-2.5 < T-score ≤ -2)
- Osteoporosis (T-score ≤ -2.5)
- Compression fracture

Pickhardt
2013

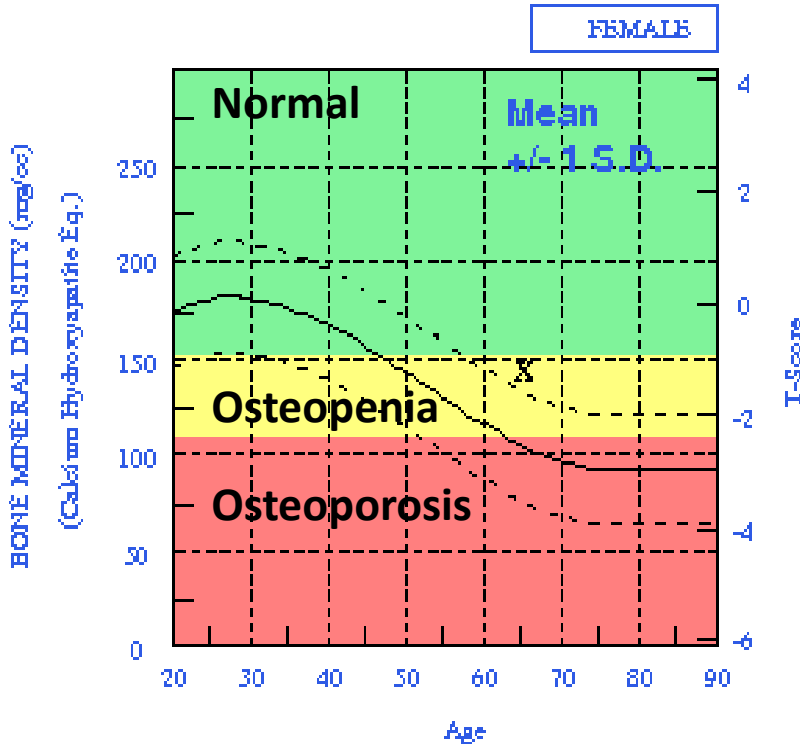
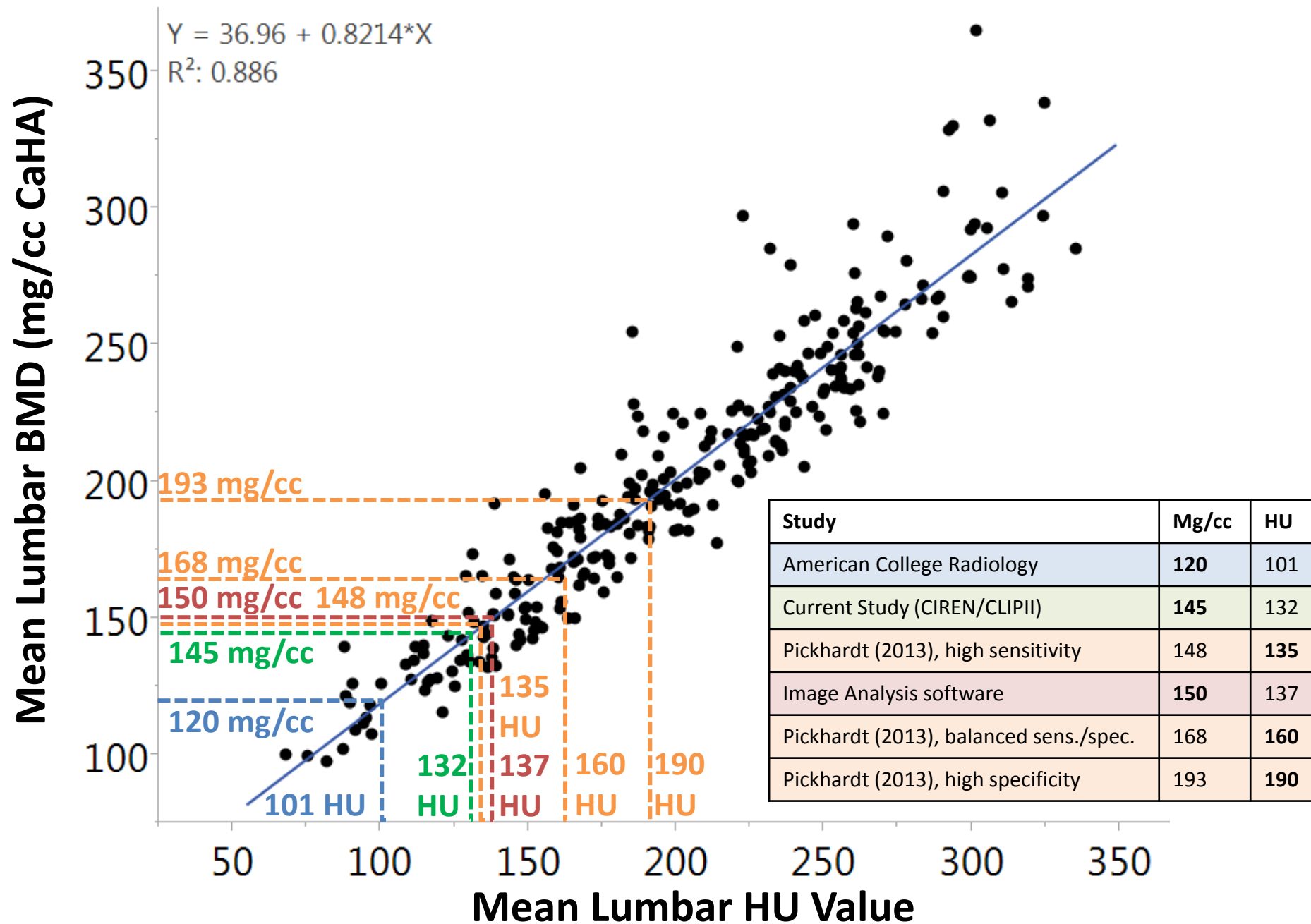
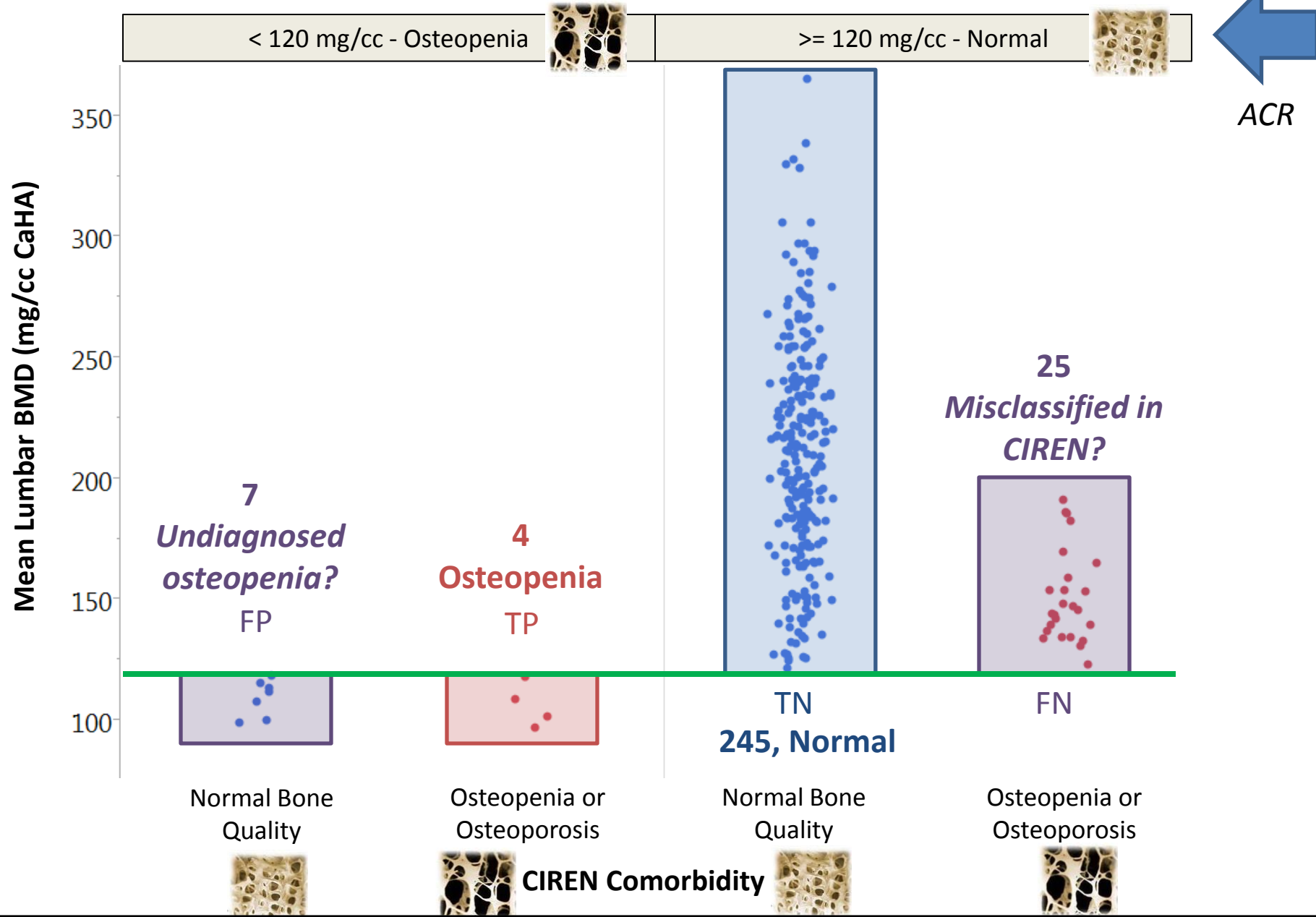


Image Analysis
Software

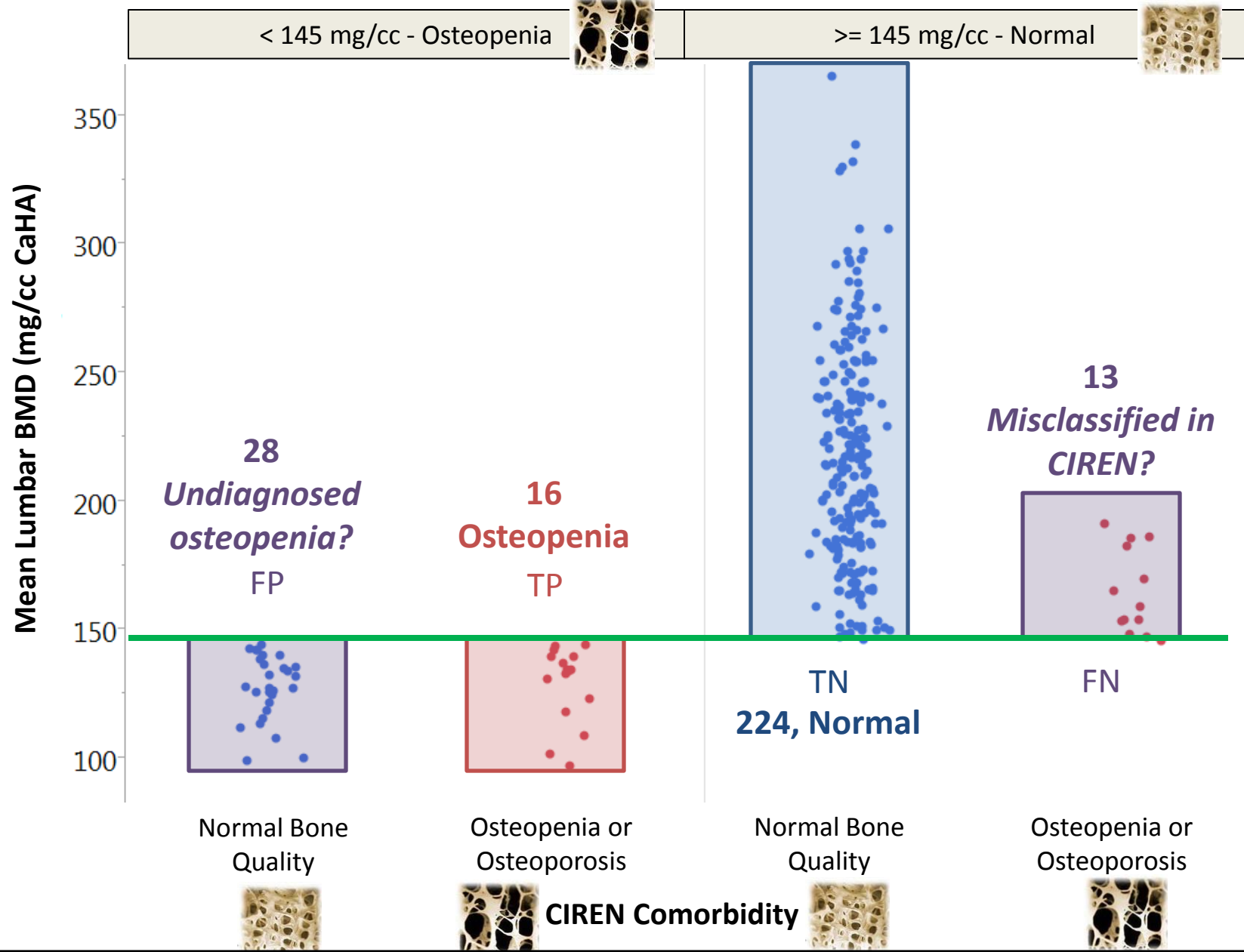
Lumbar HU vs mg/cc Relationship in CIREN subjects



CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction

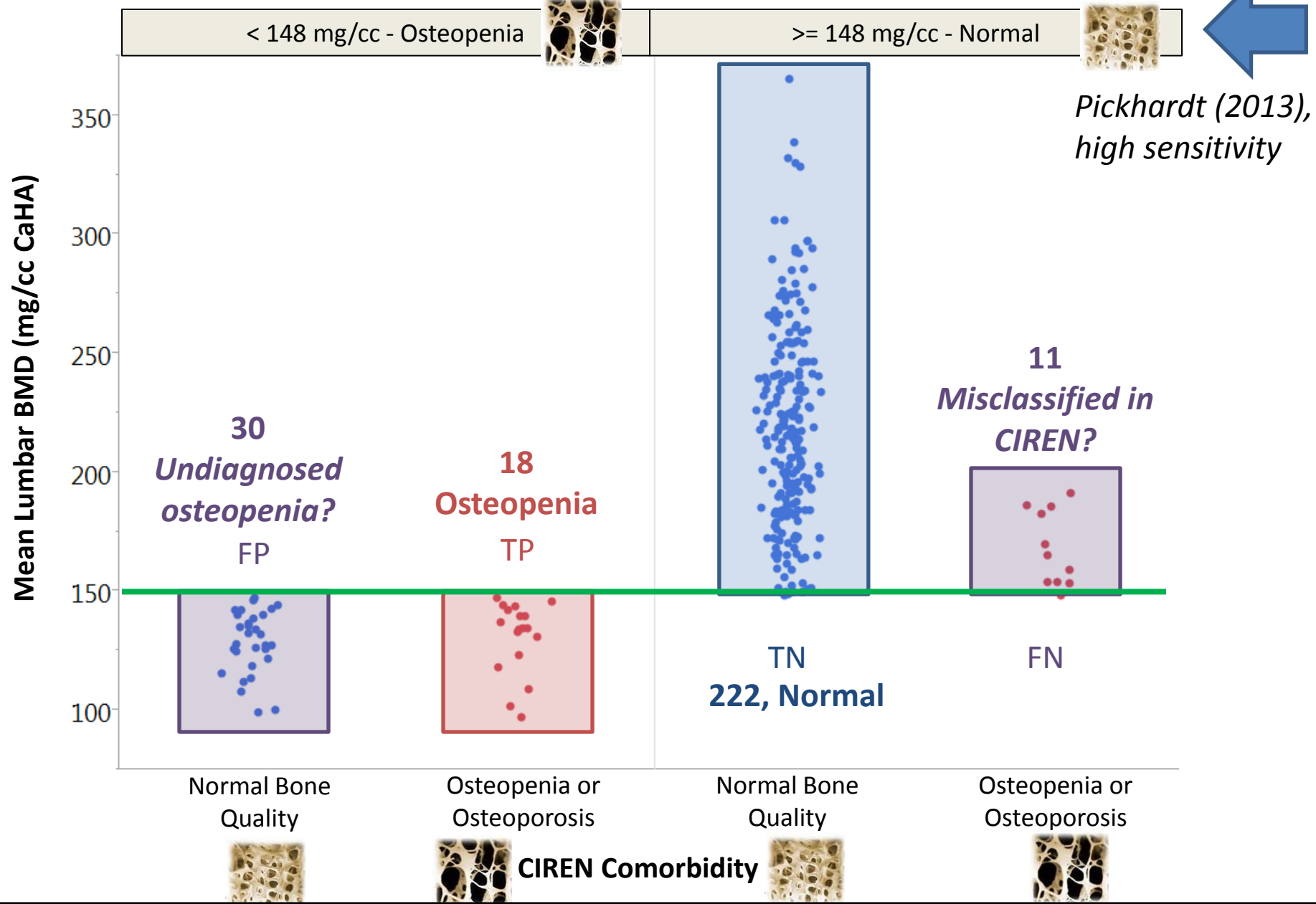


CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction

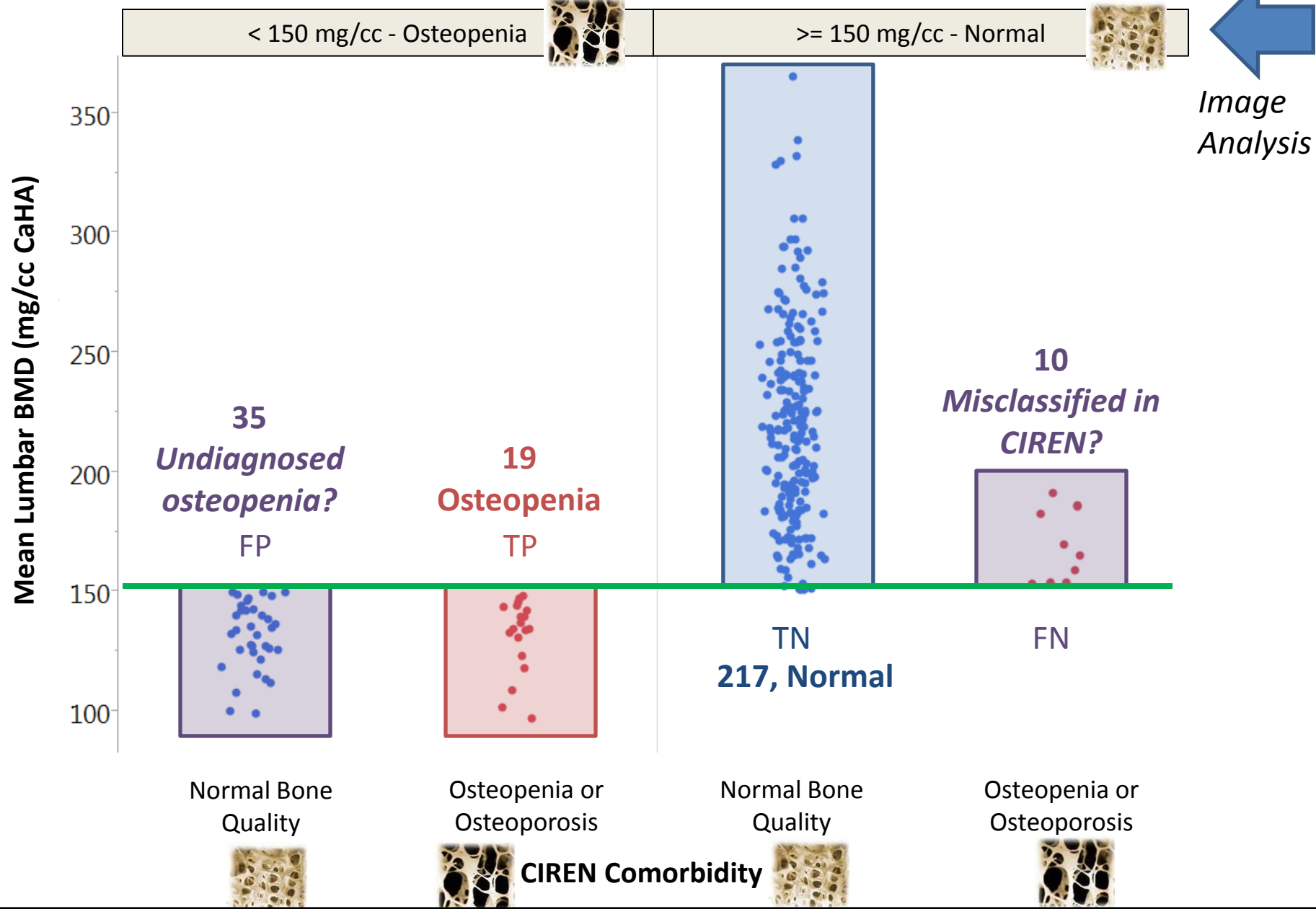


Current Study

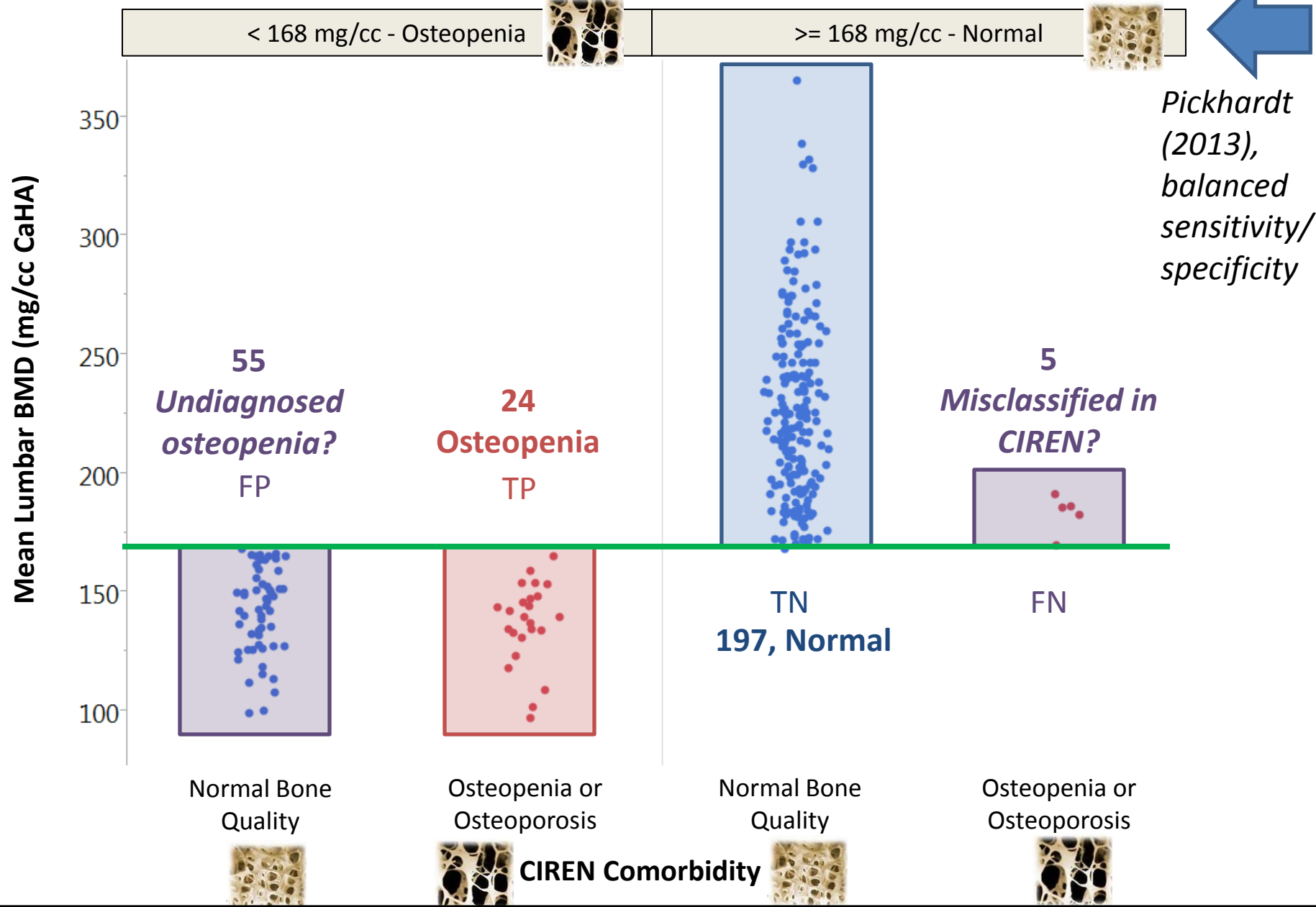
CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



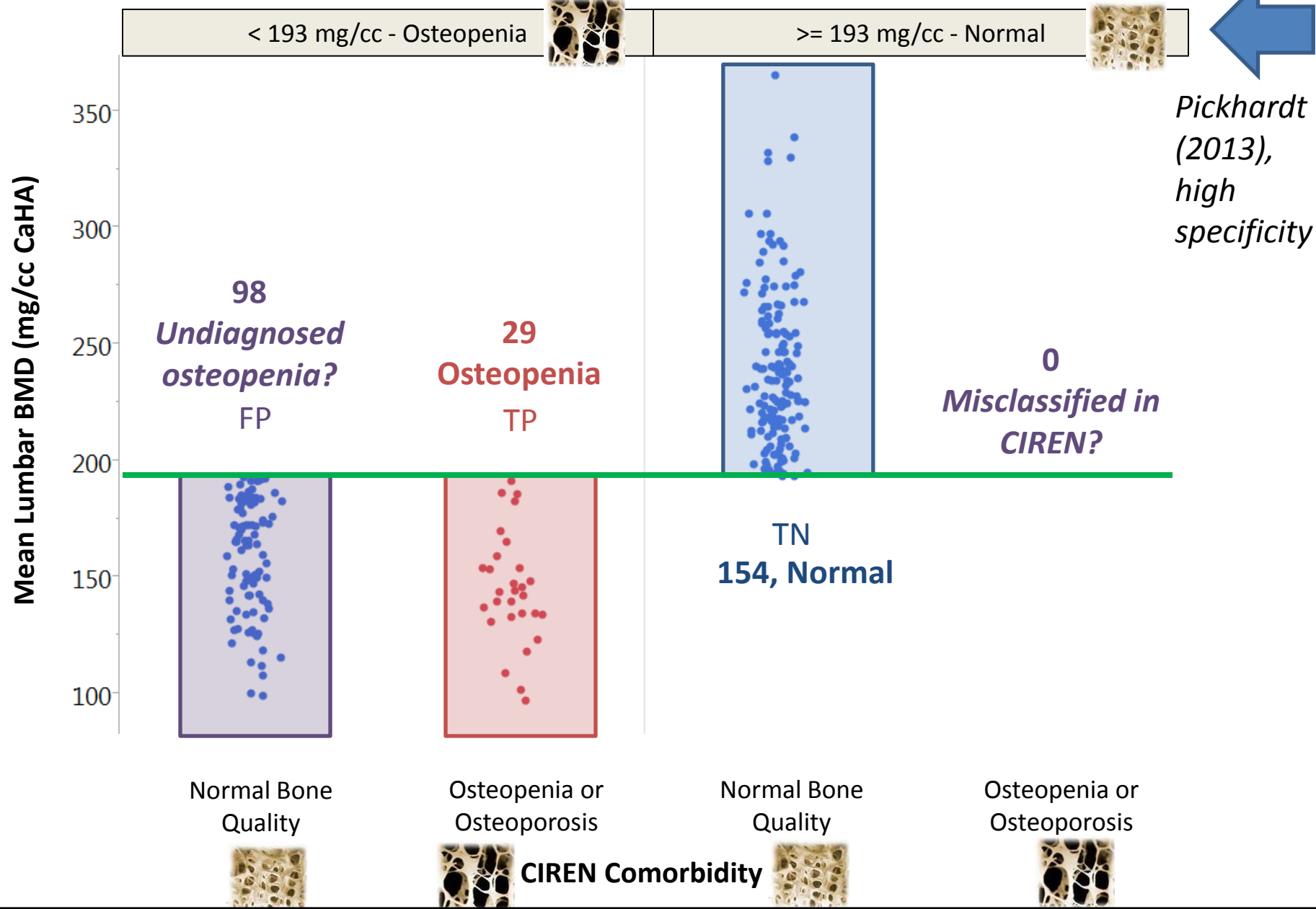
CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



CIREN Truth Table of Bone Quality: Documented Comorbidities vs CT-Prediction



CT Scanner Calibration

CT technicians perform routine calibration scans for the ED CT scanner:

- Air (at least daily)
- Water phantom (at least yearly)

Associated Errors, ED CT Scanner Calibration Reports with Water

Year	Noise CT #s	CT# (Mean +/- SD)
2005	3.20	-0.30 +/- 3.67
2006	3.77	3.70 +/- 3.77
2007	4.35	1.11 +/- 4.35
2008	4.18	3.30 +/- 4.18
2009	4.01	2.04 +/- 4.01
2011	4.40	6.32 +/- 4.40
2013	3.70	2.93 +/- 3.70
Average	3.94	2.73 +/- 4.01

QA Torso phantom:
CaHA and water
densities



INTable Calibration Phantom

http://www.image-analysis.com/intable_phantom

Associated Error of BMD Estimation from Phantom-less CT

- CT calibration reports reveal errors < 4 CT #s
 - Minimal effect on BMD estimation
 - Less than the variation in mg/cc or HU thresholds for osteopenia in the literature
- Potential improvements
 - Include a phantom in the ED CT scanner for more accurate BMD estimation
 - Daily calibrations with water or other phantoms
 - However we feel good about simple measurement using Image/J to assist with classification for CIREN subjects

Summary & Conclusions

- Phantom-less CT BMD Estimation Technique:
 - ImageJ ROIs: L1-L5, fat, muscle
 - Calibrate L1-L5 HU to mg/cc using fat-muscle ROIs & assuming -69 (fat) & 77 (muscle) mg/cc values
 - Osteopenia indicated for Lumbar BMD < 145 mg/cc
- Technique can be used for future analysis to assist with osteopenia/osteoporosis classification of CIREN occupants
 - Prospective / Retrospective
 - Other CIREN centers

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Summary & Conclusions

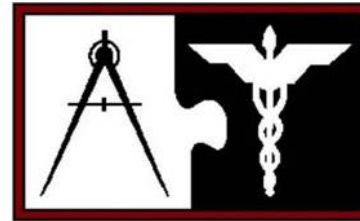
- 145 mg/cc threshold in CIREN occupants:
 - Associated with increased # rib fxs
 - 28 possible cases of undiagnosed osteopenia
 - 63% false discovery rate – ~63% of those classified as osteopenic using this technique are undiagnosed in CIREN
 - 37% PPV – Only 37% classified as osteopenic using this technique are correctly classified in CIREN
 - 13 false negatives - possible misclassifications of osteopenia/osteoporosis comorbidity
 - 45% CIREN occupants with osteopenia/osteoporosis comorbidity were classified as having normal bone quality using this technique

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Acknowledgments

Thank you!

National Highway Traffic Safety Administration



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